A DISSERTATION ON

"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''

Submitted to

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERISTY
CHENNAI

In Partial fulfillment of the Regulations
For the Award of the degree

M.D. DEGREE BRANCH VIII
RADIODIAGNOSIS

MADRAS MEDICAL COLLEGE,
CHENNAI.

MAY - 2019

CERTIFICATE

This is to certify that the dissertation titled **" T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI''** submitted by **Dr.HARISH.G,** appearing for **M.D.RADIODIAGNOSIS** degree examination in May 2019, is a bonafide record of work done by him, under my guidance and supervision in partial fulfillment of requirements of The Tamilnadu Dr. M.G.R Medical University, Chennai. I forward this to The Tamilnadu Dr. M.G.R Medical University, Chennai.

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DECLARATION

I, **Dr. HARISH.G,** certainly declare that this dissertation titled, **" T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI''** represent a genuine work of mine, done at the Barnard Institute of Radiology, Madras Medical College and Rajiv Gandhi Government General Hospital, under the supervision of **Prof.R.Ravi, M.D., D.M.R.D**., Director & Professor, Barnard Institute of Radiology, Madras Medical College and Rajiv Gandhi Government General Hospital.

I, also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, neither in India or abroad. This is submitted to The Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.D Degree in Radiodiagnosis (Branch VIII).

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ACKNOWLEDGEMENT

I would like to express my deep sense of gratitude to **the Dean**, **Professor R.JAYANTHI, M.D., FRCP.,** Madras Medical College and **Professor Dr.R.Ravi, M.D.R.D., D.M.R.D., our Director, Barnard Institute of Radiology, MMC & RGGGH, & my guide** for allowing me to undertake this study on **" T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI''** and utilize the institutional facilities.

I am also extremely indebted to **Professor Dr.N.Kailasanathan, M.D.R.D**., **D.M.R.D.,** our former Director, for his valuable suggestions, personal attention and constructive criticism during my study.

I was able to carry out my study to my fullest satisfaction, thanks to the guidance, encouragement, motivation and constant supervision extended to me, by my beloved **Head of the Department, Professor Dr.K.Malathi, M.D.R.D., D.M.R.D.** Hence my profuse thanks are due for her.

I would like to express my deep gratitude and respect to **Professor Dr.S.Babu Peter M.D.R.D., DNB,** whose advice and insight was invaluable to me. This work would not have been possible without his guidance, support and encouragement.

My sincere thanks to **Professor Dr.S.Kalpana** for her valuable support throughout the study and I also thank **Professor Dr.D.Ramesh** for his practical comments and guidance especially at the inception of this study.

I am bound by ties of gratitude to my respected Associate Professors, **Dr.E.Manimekala,** and **Dr.Shiva shankar** and Assistant Professors, **Dr.Geetha.G,**

Dr.Iyengaran.H, Dr.Mohideen Ashraf, Dr.Saranya.M, Dr.Balan.M.P, Dr.Dheebha, Dr.Karthik, in general, for placing and guiding me on the right track from the very beginning of my career in Radio diagnosis till this day.

I also thank **my past and present fellow postgraduates** who helped me in carrying out my work and preparing this dissertation. I thank **all the Radiology technicians, Staff Nurses and all the Paramedical staff members** in Barnard Institute of Radiology, for their fullest co-operation. I thank my statistician **Mr.Venkatesan**, who rendered his valuable timely help in completing this study.

I thank my **lovable parents and my sister** for their constant and persistent support for my studies and in all my endeavours.

I would be failing in my duty if I don't place on record my sincere thanks to those **patients and their relatives** who in spite of their sufferings extended their fullest co-operation to this study.

- **Dr.Harish.G**

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"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''

1. INTRODUCTION

Osteoarthritis (OA) is the most prevalent chronic disease in the elderly. Osteoarthritis is a disease attributed to multiple etiological factors and is characterized by progressive degeneration and eventual loss of cartilage tissue[(1)]. OA is still poorly understood, which may be attributed to the fact that it is generally detected at an advanced stage.

Osteoarthritis is the most common form of arthritis, with major implications for individual and public health care without effective management available. The prevalence of OA is increasing with the raise in the incidence of obesity. OA occurs when there is an alteration in the equilibrium between cartilage breakdown & cartilage repair, which will cause pain, physical & psychological distress.

Sophisticated imaging methods has helped in the development of more knowledge, and large longitudinal studies that will aid in understanding of the natural course of the disease. The field of joint and cartilage imaging, and particularly magnetic resonance (MR) imaging, has developed rapidly because of advances in technical aspect and the application of these techniques in clinical research.

In joint imaging, imaging of the articular cartilage is at the forefront. Compositional MR imaging of articular cartilage ultrastructure has given us a better understanding of the early and potentially reversible pathologic processes, which may help us to prevent the long-term morbidity of OA.

To assess the collagen network and proteoglycan content in the knee cartilage matrix, compositional imaging techniques like T2 mapping, delayed gadolinium-enhanced MR imaging of cartilage (or dGEMRIC), T1ρ imaging, sodium imaging, and diffusion-weighted imaging are available[(2)]. These methods can be used in varying combinations and at various magnetic field strengths in clinical and research settings to improve the characterization of changes in articular cartilage.

Collagen and proteoglycan-associated glycosaminoglycans are the major components of articular cartilage and are important to preserve the functional and structural integrity of cartilage. Compositional MR imaging assessment of cartilage is focused on its molecular status, specifically in regard to its collagen and glycosaminoglycan content.

2. RATIONALE OF THE STUDY

Plain x rays have been used in the evaluation of OA, which depict only narrowing of the joint space or gross osseous changes that tend to occur late in the disease. Early degenerative changes in the articular cartilage may not be visible on plain x rays. Plain x rays are not sensitive to focal loss of articular cartilage, and widening of the joint space in spite of significant loss of articular cartilage can occur in one compartment of the knee simply as a result of narrowing in the other compartment.

Magnetic resonance imaging (MRI) has been found useful to visualize cartilage directly yet morphologic imaging shows damage at a stage when cartilage is already irreversibly lost. MR imaging sequences for dedicated cartilage imaging include fat-saturated T2-weighted, proton density-weighted fast spin echo (FSE) sequences and T1-weighted spoiled gradient echo (SPGR) sequences. These sequences are inconclusive in quantifying early degenerative changes, especially biochemical alterations like proteoglycan (PG) loss.

Early events in cartilage loss include molecular changes in collagen, changes in water content & loss of proteoglycans[3]. Therefore early detection of cartilage injury would require the ability to noninvasively detect changes in PG concentration and collagen integrity before gross morphologic changes occur.

X ray and Pain scores have only a weak correlation with disease severity and symptoms. MRI provides good tissue contrast to detect morphological changes in cartilage where X ray cannot. However, physiological and bio chemical changes in

cartilage prior to morphological changes cannot be detected with conventional MRI. Detecting these changes is important because managing disease at its earliest stages can prevent morbidity to the patient.

T2 relaxation reflects the ability of free water proton molecules to move and to exchange energy inside the cartilaginous matrix. The extracellular matrix in the articular cartilage provides a motion-restricted environment to water molecules. Previous studies have shown that the water content in OA affected cartilage may increase by around 10%. Damage to collagen - PG matrix and increase of water content in degenerating cartilage may increase T2 relaxation times. Initial studies in human subjects showed elevated T2 values in patients with OA[4-8].

Many cartilage re-surfacing procedures and disease modifying drugs for OA have emerged. This prompts the need for development of non invasive imaging technique like T2 mapping to monitor early cartilage degeneration and to compare the T2 values between normal subjects & OA patients, which can be helpful in assessing the disease progression & treatment response.

3. REVIEW OF LITERATURE

EMBRYOLOGY OF THE KNEE JOINT

The elements that constitute the knee joint begin to chondrify at 6 weeks of intra uterine gestation. At 7 weeks the chondrification of the femoral condyles and tibia and fibula is well advanced. Vascular canals invade the patella, femur, and tibia around the 12th week[9]. At 14 weeks, enchondral ossification of femur and tibia has reached the metaphyseal areas. Chondrocyte columns are formed at 18 weeks[10].

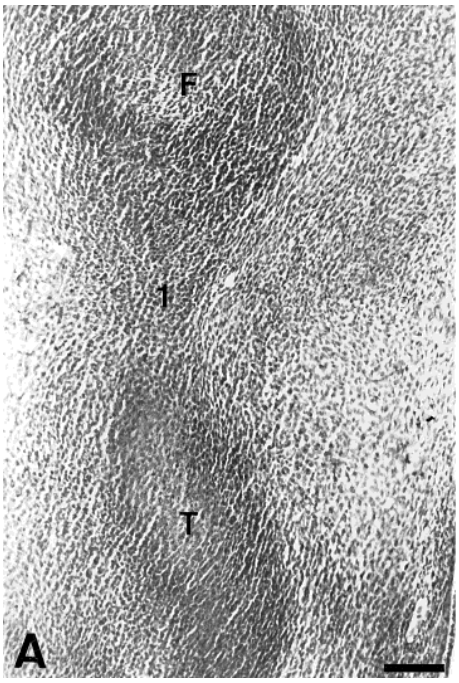

Fig 3.1 A : The epiphysis of the femur (F) and tibia (T) begin their chondrification. Between them is the articular inter zone of the knee (1).

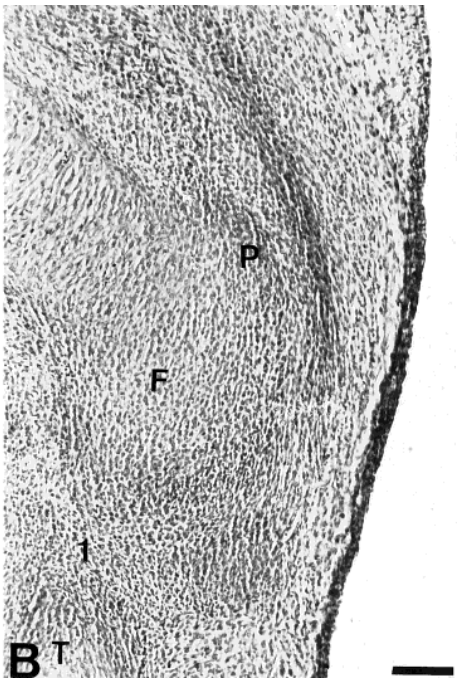

Fig 3.1 B : Ventrally to the femur, the organization of the patella (P) begins as a dense blastema.

A uniform inter zone between femur and tibia is present at 6 weeks.

Joint cavitation starts at 8 weeks at the patellofemoral level. The cavitation of the femorotibial compartment begins first between femur and menisci at nine and a half weeks and is seen between menisci and tibia shortly after.

Collateral ligaments are formed at 7 weeks. Cruciate ligaments are well developed at 9 ½ weeks. Menisci are formed from 9 ½ weeks. At 20 weeks menisci contain a dense fibrous tissue & richly vascularised rim. Medial & lateral patellar retinaculum are formed around 10 weeks. At 14 weeks identification of various muscles is possible.

The formation of the anterior tibial tuberosity merits special attention. At 12 weeks a vascular channel invades the proximal tibial cartilage anlage in an upward and oblique direction and starts to separate a tongue-shaped cartilage from the epiphysis ; 2 weeks later the vessel has grown in deeper. By 18 weeks the formation of the tuberosity is better outlined ; it is well defined at 20 ½ weeks. When the fetus has reached the 20th week of gestation, all anatomic structures found during the postnatal period are easily recognizable.

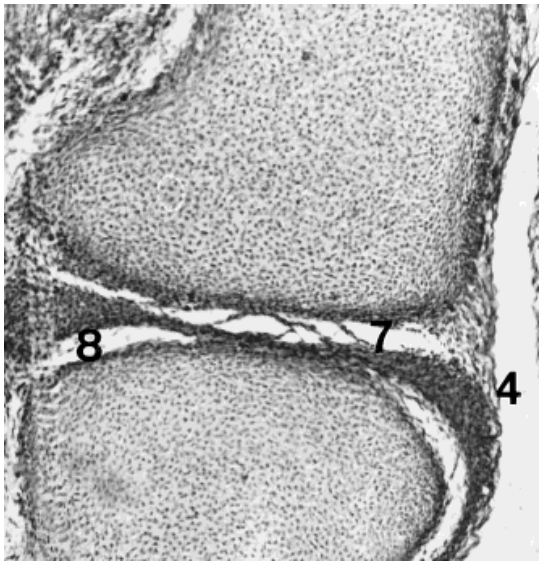

Fig 3.2 A : Formation of the meniscofemoral (7) and meniscotibial (8) knee joint cavities has begun. Both cavities are crossed, at this time, by mesenchymal trabeculae. Knee joint capsule (4) is attached to the eccentric margin of the menisci.

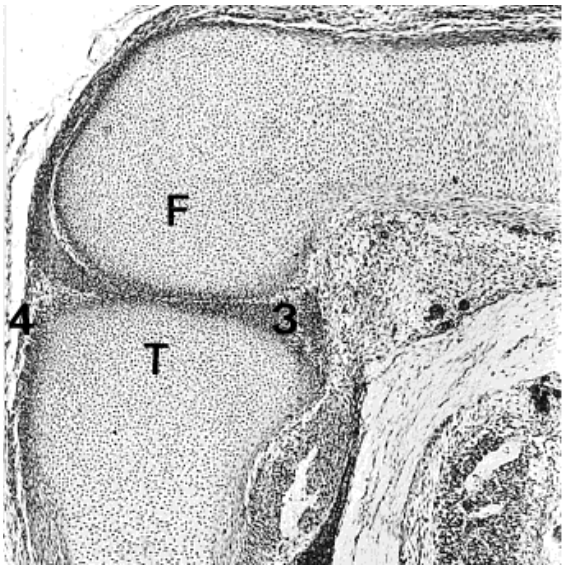

Fig 3.2 B : The lateral portions of the articular interzone of the knee form the menisci (3) that are located between the condyles of the femur (F) and tibia (T). The knee joint capsule (4) is attached to the eccentric margin of the menisci

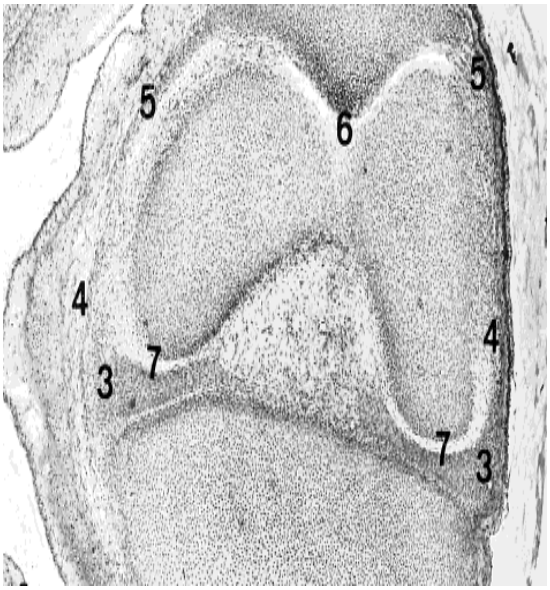

Fig 3.3 A : The femoropatellar (6) and meniscofemoral (7) cavities are observed. The knee joint capsule (4), attached to the eccentric margin of the menisci (3), is strengthened by the condylopatellar ligaments (5).

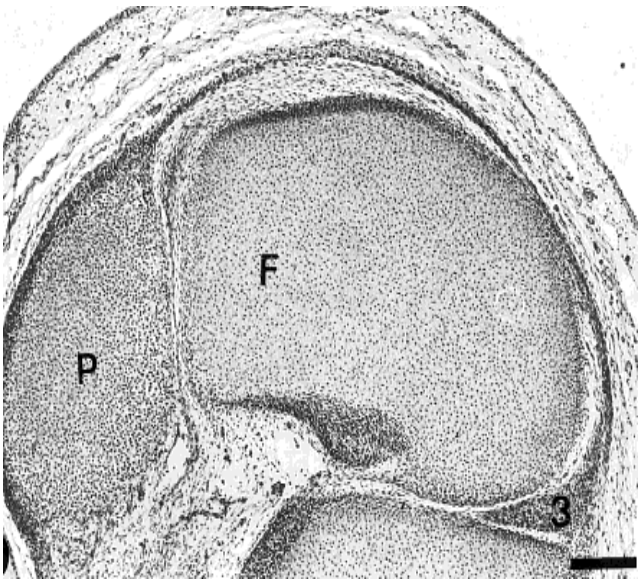

Fig 3.3 B : The patella (P) is basically articulated with the lateral condyle of the femur (F). Below the patella, a triangular space forms. This space is occupied by a mesenchymal tissue that gives rise to the intraarticular pad of fat. Lateral meniscus (3).

ANATOMY OF THE KNEE JOINT

The knee joint is a synovial joint & is the largest synovial joint in the body. It consists of articulation between femur & tibia which is weight bearing and between patella & femur, which allows the pull of quadriceps femoris over the knee to tibia. Two fibro cartilaginous menisci between femoral condyles and tibia accommodate changes in the shape of articular cartilage during movements.

The knee joint is a hinge joint allowing mainly flexion & extension. They are reinforced by the collateral ligaments, one on each side of the joint. The cruciate ligaments connect the ends of femur & tibia. The joint has an efficient locking mechanism to reduce the muscle energy required to keep the joint extended when standing [11].

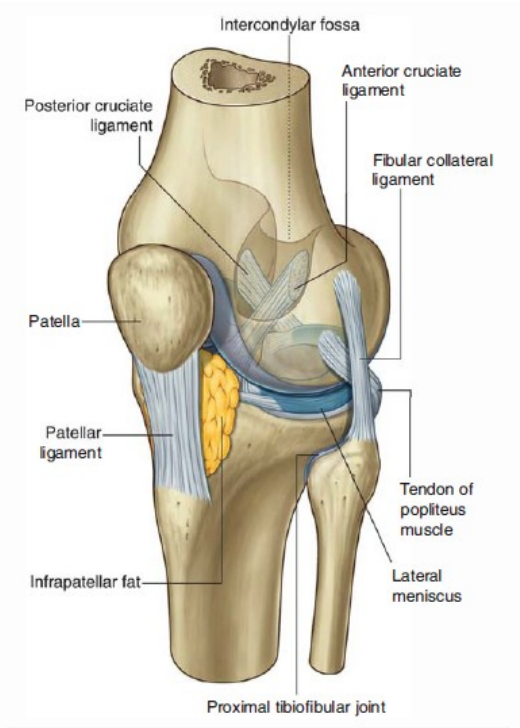

Fig 3.4 : The knee joint.

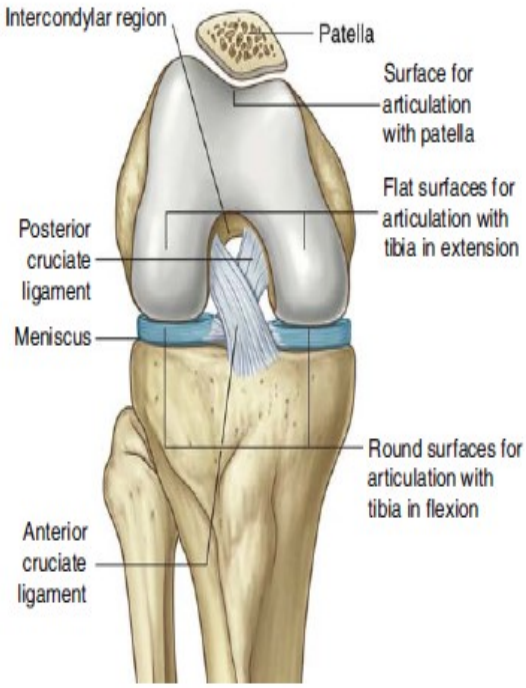

Fig 3.5 : Articular surfaces of knee joint

MENISCI :

There are two menisci, the medial & lateral. They are fibrocartilaginous C shaped cartilages, attached at each end to facets in intercondylar region of tibial plateau.

The medial meniscus is attached to the joint capsule & to the tibial collateral ligament, whereas the lateral meniscus is attached to popliteus muscle tendon & unattached to the capsule, hence it is more mobile. The menisci are interconnected anteriorly by the transverse ligament. The menisci improve the congruency between the femoral & tibial condyles during movement.

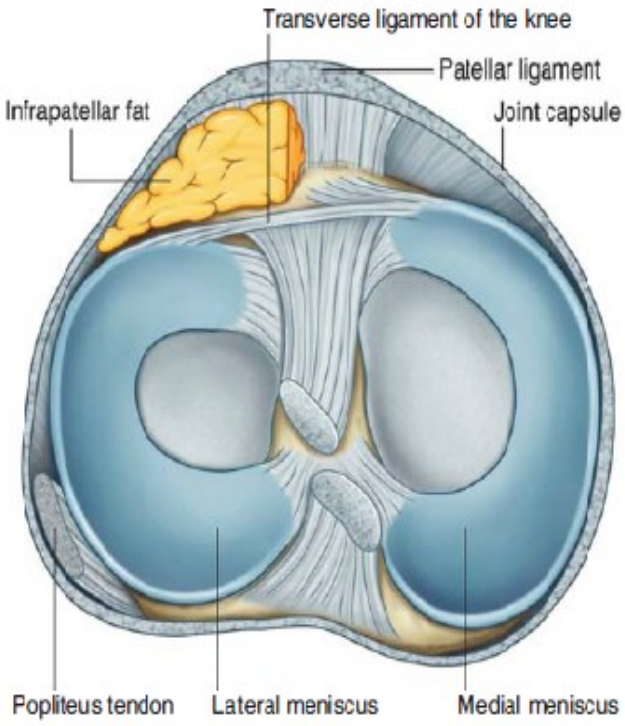

Fig 3.6 : Superior view of the menisci of the knee joint

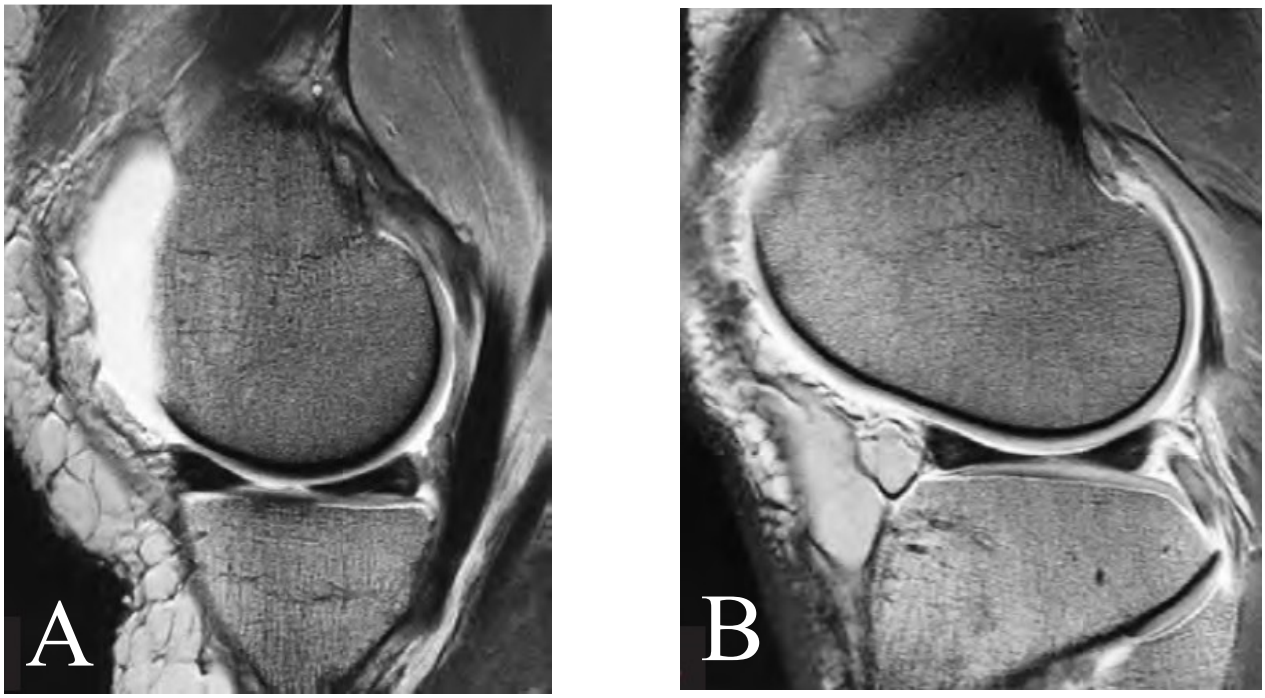

Fig 3.7 : Sagittal MR arthrographic images showing normal medial (A) and lateral (B) meniscus [12].

COLLATERAL LIGAMENTS :

The fibular collateral ligament or lateral collateral ligament (LCL) is cord like & is attached superiorly to lateral femoral epicondyle and inferiorly to a depression on the lateral surface of fibular head.

The tibial collateral ligament or medial collateral ligament (MCL) is broad and flat and is attached superiorly to medial femoral epicondyle just inferior to adductor tubercle and inferiorly to medial surface of tibia behind the attachment of Sartorius, gracilis and semitendinosus tendons.

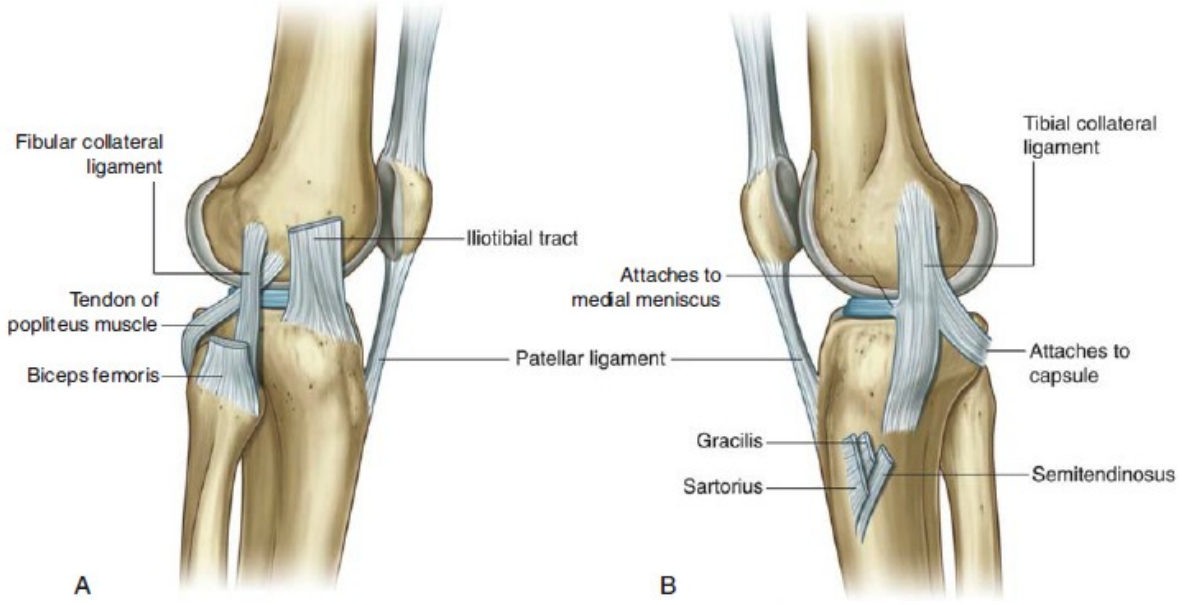

Fig 3.8 : Collateral ligaments of knee. Lateral view (A) and medial view (B)

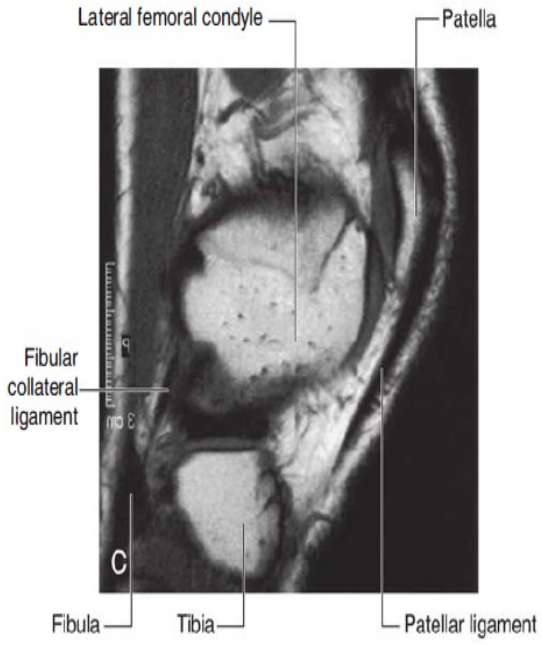

Fig 3.8 C : Sagittal T1 weighted MR image showing normal fibular collateral ligament & patellar ligament

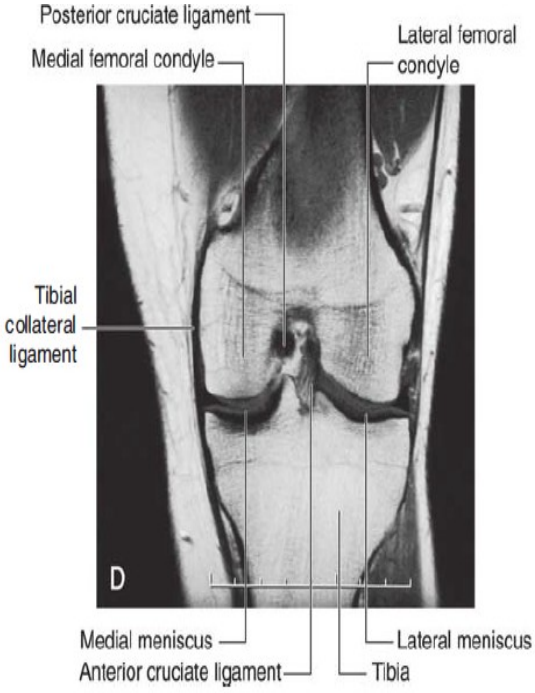

Fig 3.8 D : Coronal T1 weighted MR image showing normal tibial collateral ligament & cruciate ligaments and menisci

CRUCIATE LIGAMENTS :

The anterior cruciate ligament (ACL) is attached to the anterior part of the intercondylar area of tibia and ascends posteriorly to attach to the lateral wall of intercondylar area of femur.

The posterior cruciate ligament (PCL) is attached to the posterior part of the intercondylar area of tibia and ascends anteriorly to attach to the medial wall of intercondylar area of femur.

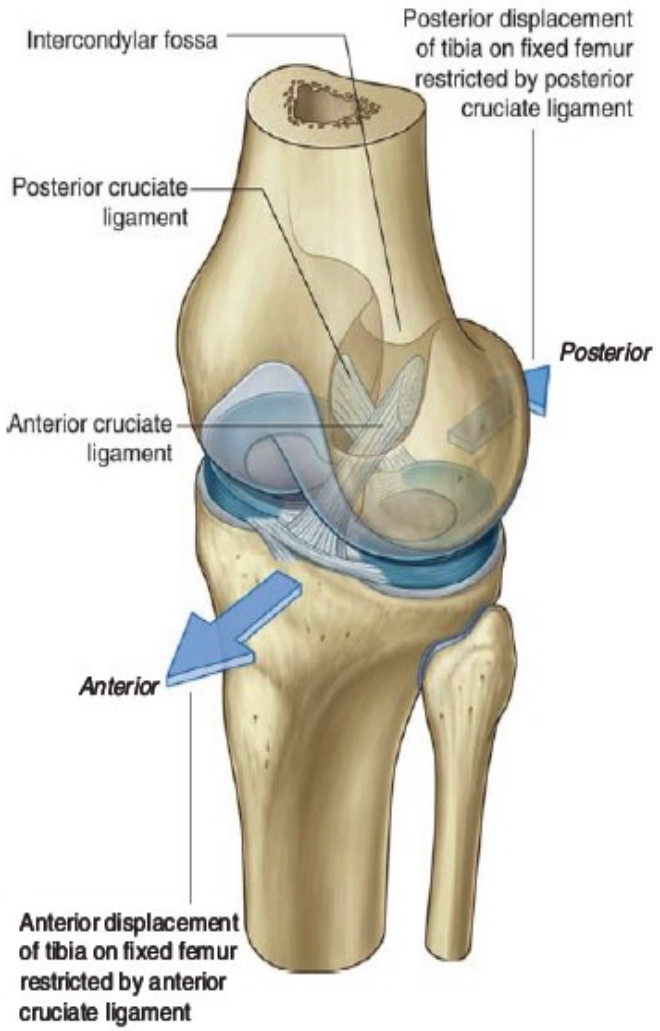

Fig 3.9 : Cruciate ligaments of the knee joint. Superolateral view.

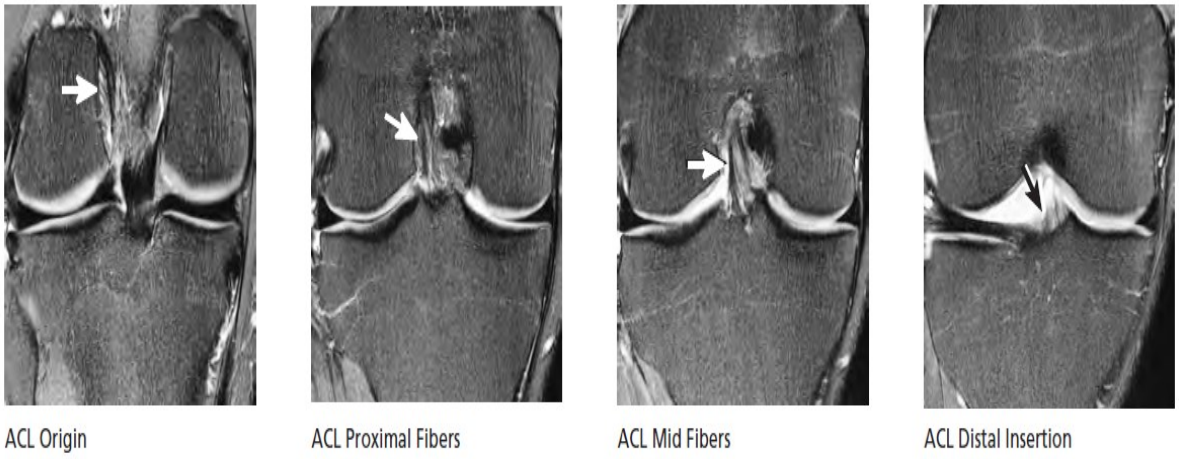

Fig 3.10: Anterior cruciate ligament

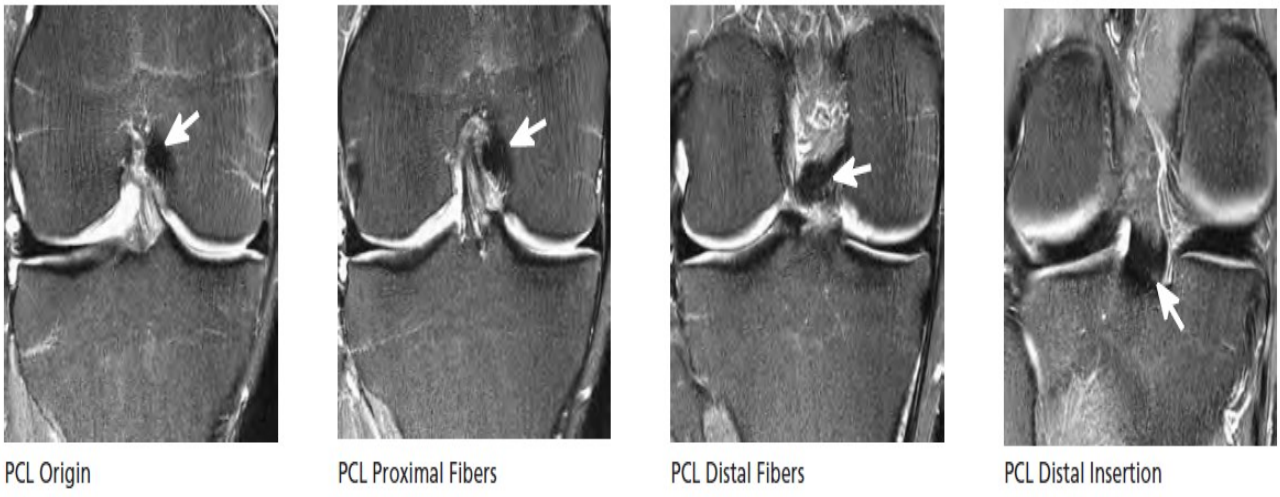

Fig 3.11: Posterior cruciate ligament

VASCULAR SUPPLY OF THE KNEE JOINT :

The major source of blood supply to the knee joint is via descending and genicular branches of femoral,popliteal and lateral circumflex femoral arteries in thigh and circumflex fibular artery and recurrent branches from anterior tibial artery arteries in leg.

IMAGING OF THE KNEE JOINT

X RAY

The common projections taken for knee joint include AP view, lateral view, intercondylar (tunnel view), tangential (skyline view)[13].

AP VIEW

Distal femur, proximal tibia and fibula, femorotibial joint space, and patella can be demonstrated. Patient is placed in supine or upright position. Upright views can be used to demonstrate joint space narrowing and femoro tibial subluxation.

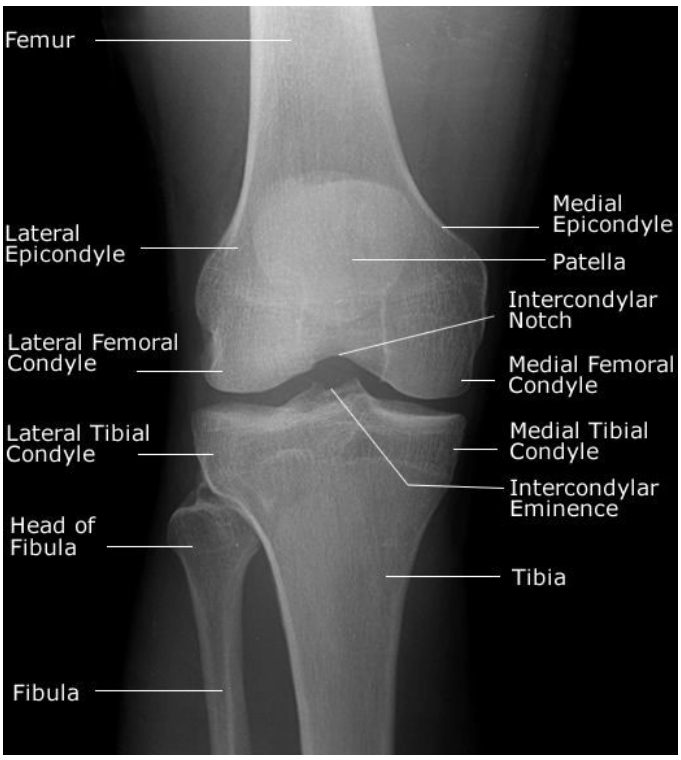

Fig 3.12: X ray knee joint : AP view

LATERAL VIEW :

Distal femur, proximal tibia and fibula, patella, and patellofemoral and tibiofemoral joint spaces can be demonstrated. Patient is placed in lateral recumbent position at 30 to 45^0 position.

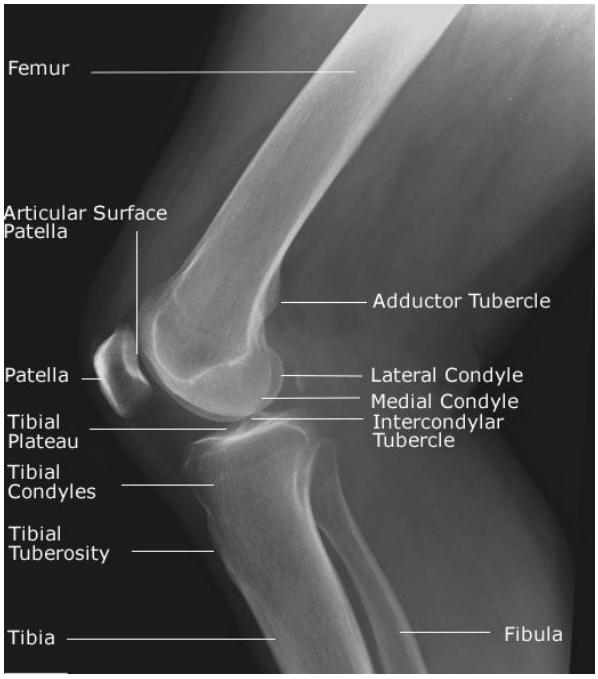

Fig 3.13: X ray knee joint : Lateral view

INTERCONDYLAR (TUNNEL VIEW) :

Intercondyloid fossa, distal femur, proximal tibia, tibial eminences, proximal fibula, and joint space can be demonstrated in tunnel view. Patient is placed in kneeling or prone position.

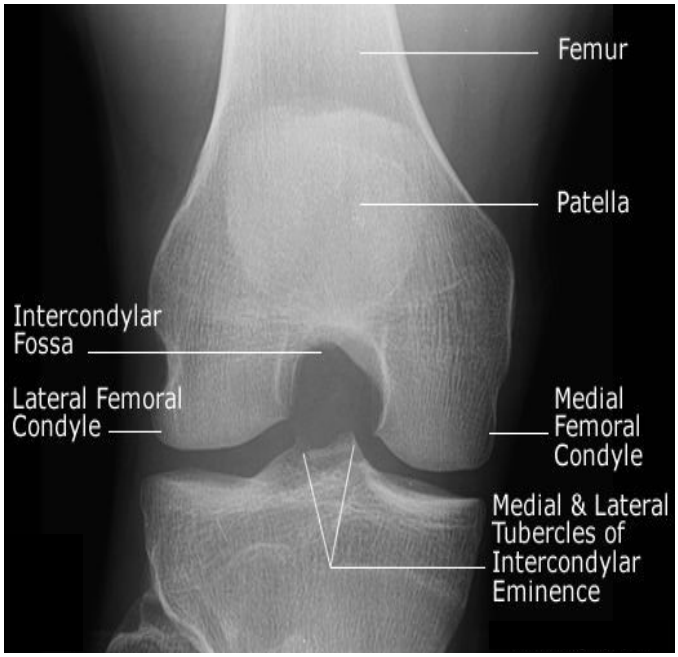

Fig 3.14: X ray knee joint : Intercondylar view(Tunnel view)

SKYLINE VIEW :

Patella and patellofemoral joint space can be demonstrated. Patient is placed in prone position with knee in full flexion.

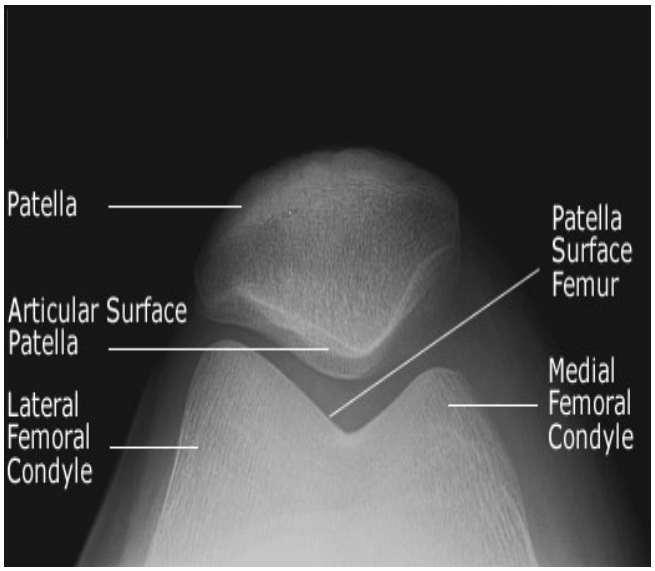

Fig 3.15: X ray knee joint : Skyline view

MRI OF THE KNEE JOINT – GENERAL IMAGING PRINCIPLES :

MRI of the knee joint is performed in the axial, sagittal, and coronal planes. There are several general principles that assist in the development of sequences for a comprehensive knee examination: A form of T2 weighting (like fat supressed proton density fast spin echo [FS PD FSE]) is used in each of the three acquisition planes - axial, sagittal, and coronal. Addition of FS helps in better visualisation of articular cartilage, fluid, edema and contusions. Sagittal T2* gradient echo (GRE) useful in detecting meniscal degeneration, patellar tendinosis and chondrocalcinosis. T1 weighted image must be acquired in at least one plane to assess the marrow fat signal intensity changes in sclerosis or edema in case of trauma, infection and neoplasia. Trochlear groove lesions are best evaluated in sagittal images. Patellar cartilage is best assessed in axial images.

Therefore the sequences routinely used in MR imaging of the knee joint include axial T1 or PD FSE, axial FS PD FSE, sagittal FS PD FSE, sagittal T2* GRE, sagittal PD FSE, coronal T1 or PD FSE and coronal FS PD FSE.

A phased-array eight-channel extremity coil provides a uniform signal-to-noise ratio (SNR) across the knee. An acquisition matrix of 256 or higher, a field of view of 12 to 14 cm, and 1 to 2 number of excitations (NEX) are routinely used. A field of view (FOV) of 12 cm or less will increase spatial resolution when scanning is done in children.

Fig 3.16: Fifteen channel transmit/receive knee coil

An axial acquisition through the patellofemoral joint is used as the initial localizer for subsequent sagittal and coronal plane images. Meniscal pathology is evaluated primarily on sagittal plane images. The meniscal root attachments are evaluated on posterior coronal images. The cruciate ligaments are best seen on sagittal plane images.

The medial and lateral collateral ligaments (MCL and LCL) are displayed on coronal and axial images and can secondarily be visualized on peripheral sagittal images. Four-millimeter sections are used for axial and coronal plane images, and 3- to 4-mm-thick sections are used for sagittal images. MR arthrography has limited application and is used primarily to identify retearing of a primary meniscal repair in the postoperative knee.

OSTEOARTHRITIS OF THE KNEE JOINT

Degenerative joint disease (DJD) or Osteoarthritis (OA) is very common in knee. This is mainly attributed to its weight bearing function & susceptibility to injury. Altered knee extension mechanisms and the use of wide-heeled shoes are some of the factors that have been implicated in the predisposition of the knee to arthritis[14,15].

There are three radiographic compartments in the knee – Medial, lateral and patella femoral. Medial femoro tibial joint is the most common compartment involved typified the decrease in medial joint space. The diminution in joint space is accurately assessed by erect weight bearing AP films. Sub chondral sclerosis is more common in tibia. Osteophytes arise from the tibial and femoral margins on the side of decreased articular space. Single or multiple loose bodies are commonly seen in femoro tibial articulation and can undergo calcification or ossification.

Sub chondral cysts are mainly located near tibial plateau[16]. On CT, gas can be demonstrated within these cysts. Varus type deformity is a late manifestation, with medial shifting of femur in relation to tibia [17].

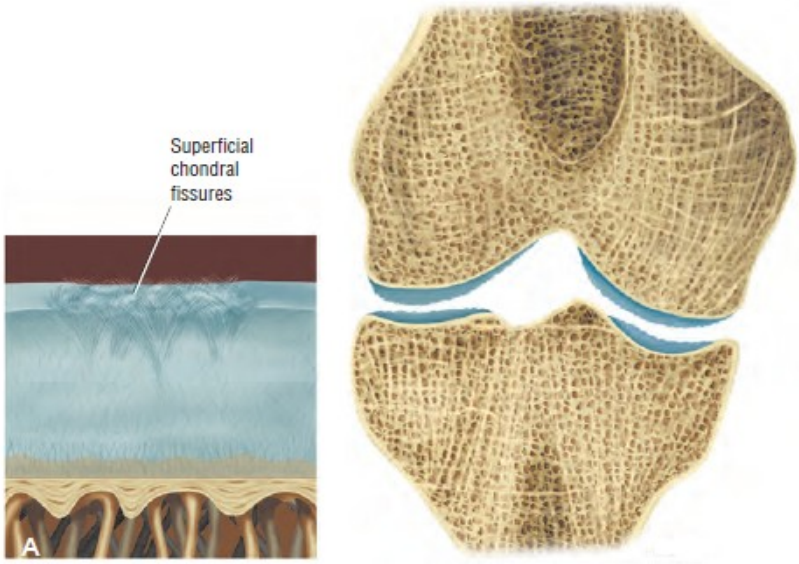

Fig 3.17 : A - Early OA of the knee showing superficial fissures in articular cartilage.

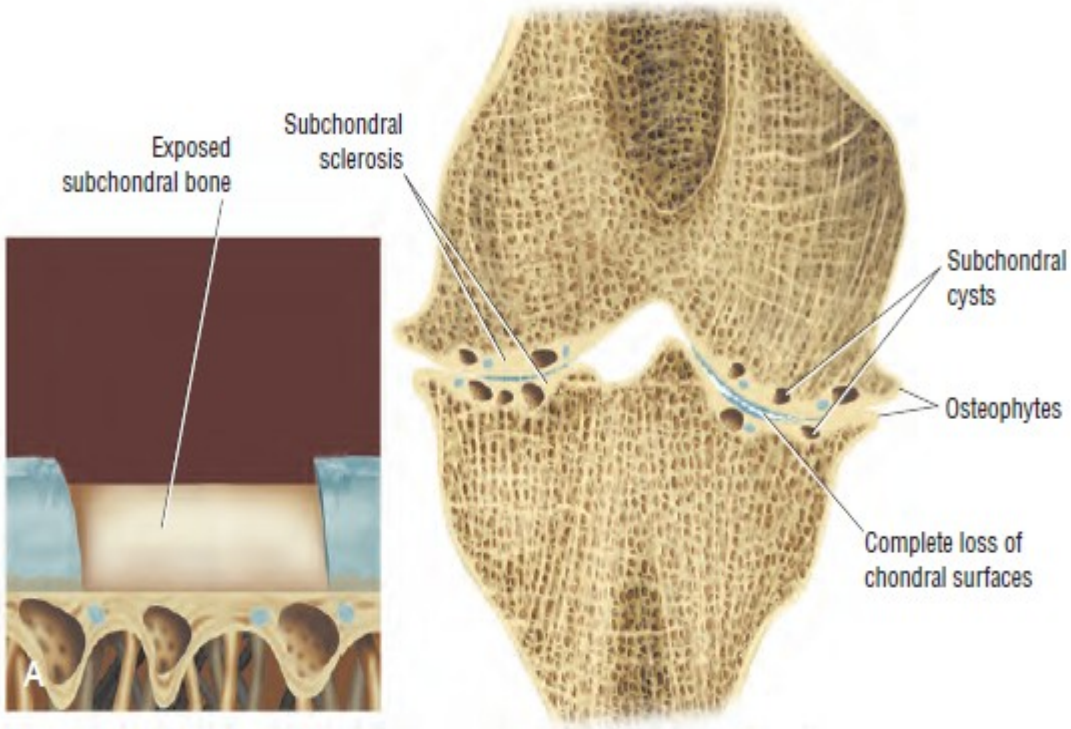

Fig 3.17 : B - End-stage degenerative arthritis showing full-thickness erosions, subchondral sclerosis, cysts, loss of joint space, and osteophytes.

Fig 3.18 A : Moderate DJD showing severe loss of medial joint space, sclerosis, and osteophytes.

Fig 3.18 B : Severe DJD showing complete loss of medial joint space, sclerosis, and osteophytes and lateral tibial shift (genu varus) .

Degenerative changes in patella femoral joint is usually found in combination with varying degrees of femorotibial DJD. Prominent signs include loss of joint space, osteophytes, sclerosis and anterior femoral erosion. In early stages loss of joint space is common in lateral aspect of the joint

A smooth well circumscribed, extrinsic erosive defect is occasionally observed in advanced patellofemoral degeneration above the superior pole of patella. Anterior patellar surface appears irregular because of bony excrescences. This is known as Tooth sign [18] .

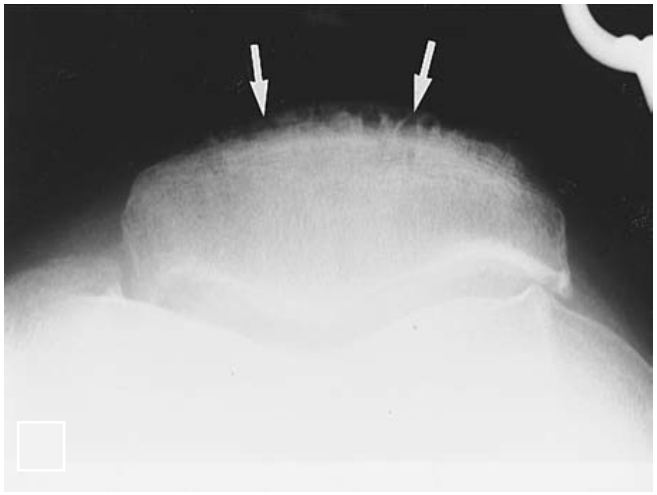

Fig 3.19 : Patellar degenerative enthesopathy (patella tooth sign) - skyline projection shows irregular bony spicules (arrows)

RADIOGRAPHIC GRADING OF OA :

The severity of OA is mainly based on joint space narrowing and concomitant subchondral bone abnormalities[19-21]. Osteophytes develop at an earlier stage than joint space narrowing. Semi quantitative scoring systems and atlases [22–24] represent specific grades of severity of radiographic OA.

Kellgren- Lawrence (KL) grading scheme is the most widely used and current accepted standard for the diagnosis of OA on radiographs [25]. The definition of radiographic OA relies on the presence of "definite" osteophytes on the anteroposterior weight bearing radiograph.

Overview of Kellgren-Lawrence Grading System for Assessment of Radiographic OA [26]

Kellgren- Lawrence Grade	Definition
0	No feature of OA
1	Doubtful joint space narrowing (JSN) and possible osteophytic lipping
2	Definite osteophytes and possible JSN
3	Moderate multiple osteophytes, definite JSN, and some sclerosis and possible deformity of bone ends
4	Large osteophytes, marked JSN, severe sclerosis, and definite deformity of bone ends

Source – Reference 21 and 26

The conventional extended-knee x ray is still to document evidence of marginal tibiofemoral osteophytes on which the diagnosis of knee OA is based. However, the extent of joint space narrowing in the presence of marginal osteophyte may not be apparent on the extended-knee view [27,28]. An alternate projection is Lyon-Schuss position with 10° caudad angulation of the x-ray beam (ie, a fixed-flexion radiograph, with or without use of a positioning frame). Two distinct advantages with this radiograph are that knee flexion is more likely to reveal cartilage loss that is common to the posterior aspect of the femur [29] and the fixed-flexion view is more likely than the extended-knee view to represent the joint space in parallel or near-parallel alignment with the x-ray beam.

MRI OF ARTICULAR CARTILAGE

MR imaging techniques used for evaluating articular cartilage these purposes can be divided into two broad categories according to their usefulness for morphologic or compositional evaluation [30,31]. The morphological evaluation of cartilage is based on the sequences that assess the structure of cartilage and morphological defects in articular cartilage. The compositional imaging of cartilage is based on sequences that evaluate the collagen network and proteoglycan content in the cartilage matrix.

The new surgical and pharmacologic agents that are available to treat the damaged articular cartilage, and the need to monitor the effects of treatment, have led to development of various MR imaging techniques that allow morphologic assessment of cartilage, cartilage volume quantification and evaluation of biochemical composition of articular cartilage [32–37].

Pharmacologic agents that are proposed to treat damage to the cartilage include dietary supplements like chondroitin and glucosamine sulfates. Reparative and reconstructive surgical techniques that are available to treat traumatic and degenerative cartilaginous damage include microfracturing and drilling, autologous chondrocyte implantation and osteochondral autologous transplantation (mosaicplasty) [38,39].

MORPHOLOGIC ASSESSMENT OF ARTICULAR CARTILAGE :

Morphological assessment techniques provide accurate information about processes like fissuring and focal or diffuse partial- or full-thickness cartilage loss. Noyes or Outerbridge scale [40,41] is used to grade cartilage lesions in the knee in clinical practice. Semiquantitative scoring methods such as those known by the acronyms WORMS (*w*hole-*or*gan *M*R imaging *s*core) [42], BLOKS (*B*oston-*L*eeds *o*steoarthritis *k*nee *s*core) [43], and KOSS (*k*nee *o*steoarthritis *s*coring *s*ystem) [44] are used in morphologic evaluation of cartilage with MR imaging in knee osteoarthritis trials.

The sequences that can be used in morphological assessment of articular cartilage are [30] ;

- 2D and 3D fast spin echo (SE)
- 3D spoiled gradient-recalled echo (SPGR)
- 3D dual-echo steady state (DESS)
- 3D balanced steady state free precession (bSSFP)
- 3D driven equilibrium Fourier transform (DEFT)
- 3D fast SE sampling perfection with application-optimized contrast using different flip-angle evolutions (SPACE)

FAT SUPPRESSION TECHNIQUES :

Fat suppression technique are used to increase the contrast between lipid surfaces and nonlipid surfaces, add dynamic range, and reduce chemical shift artifacts. These techniques provide increased contrast at the subchondral bone–cartilage interface. Fat saturation is a commonly used technique, that involves the excitation and dephasing of the spinning protons in fat by a lipid-specific radiofrequency pulse applied before each repetition of a 2D or 3D SE or GRE imaging sequence.

The drawback of using fat saturation technique in combination with the 3D GRE sequences is that it lengthens the acquisition time [(45)]. Iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) provides uniform fat suppression in the challenging magnetic field environments of knee imaging while maintaining a high signal to noise ratio (SNR).

This technique is based on the use of asymmetric echoes and least squares fitting to maximize SNR performance[(46)], and it can be used in along with either an SE or a GRE sequence. Spectral excitation technique in which only water spins in a surface are excited can be used as an alternative option [(47)].

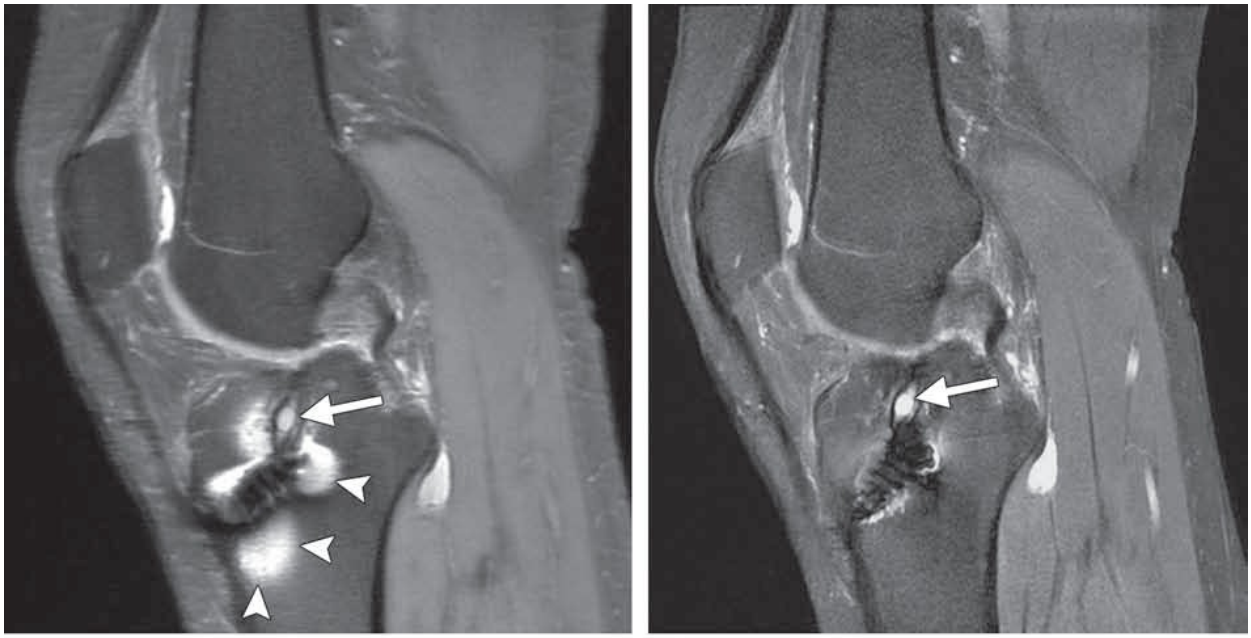

Fig 3.20 : (a) Sagittal intermediate-weighted fat-saturated fast SE image (TR msec/echo time [TE] msec = 4000/35) shows regions of high signal intensity due to poor fat saturation (arrowheads) adjacent to a tibial interference screw (arrow). (b) Sagittal intermediate-weighted IDEAL fast SE water image (TR/TE = 4000/35) depicts a cyst adjacent to the interference screw (arrow). The signals from fat and water are better differentiated with this technique.

Short inversion time inversion recovery (STIR) imaging can also be used for assessing areas affected by magnetic field inhomogeneity. This technique provides fat suppression allowing accurate depiction of cartilaginous defects in the knee joint .
It is commonly used for that purpose, even in large knee osteoarthritis trials [48]. Water excitation imaging with short TR (18 msec) and a small flip angle (15°–40°) is based on the selective excitation of non–fat-bound protons is usually used to depict cartilage

with high signal intensity and high contrast to surrounding tissue. Reduced acquisition time and ameliorated chemical shift artifacts are the advantages of this technique.

TWO-DIMENSIONAL SE AND FAST SE IMAGING :

T1-weighted, proton density– weighted, and T2-weighted imaging sequences with or without fat suppression are the most commonly used sequences in the assessment of joint cartilage. Intra substance anatomic detail of hyaline cartilage [49] are well depicted in T1-weighted images but do not provide good contrast between joint effusion and the cartilage surface. This limits their usefulness in the assessment of focal cartilaginous defects.

T2-weighted imaging provides good contrast between the cartilage surface and joint effusion, which can detect focal areas of delamination or other defects. Weakening of internal cartilage signal as some components of cartilage have short T2 is the major drawback of T2 weighted imaging. Intermediate weighted sequences with a TE of 33 – 60 msec provides higher cartilage signal intensity than standard T2. This technique combines the contrast advantage of proton density (PD) weighting with T2 weighting. PD and T2 weighted imaging are useful in the morphological assessment of articular cartilage, menisci and ligaments. The use of these techniques in knee osteoarthritis trials has lead to the detection of various risk factors for the progression of disease over time [50] and is recommended by international cartilage repair society [51].

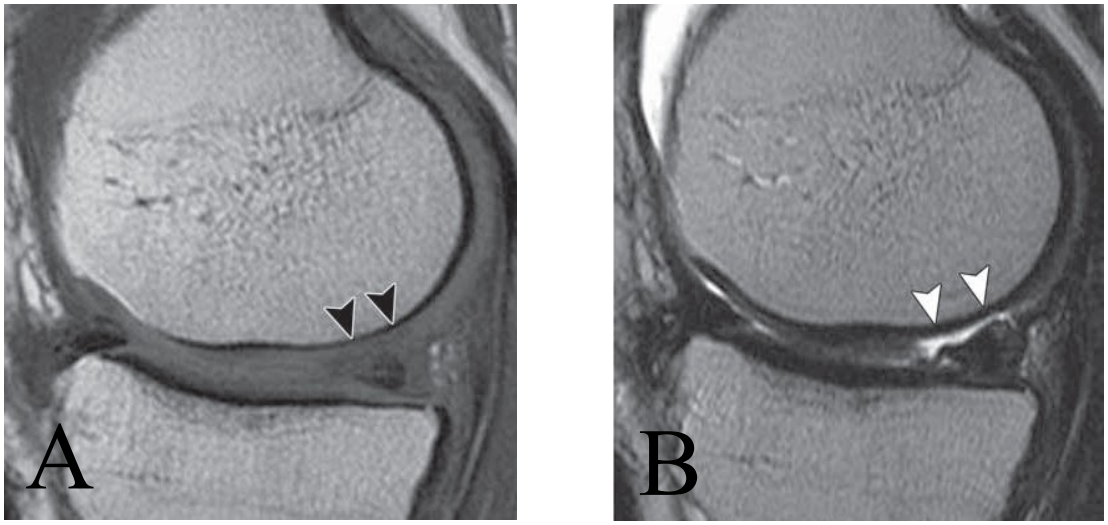

Fig 3.21 : A) T1 weighted image with poor contrast between synovial fluid and cartilage. B) T2 weighted image showing cartilage defect. Better contrast than T1 weighted image noted between synovial fluid and cartilage.

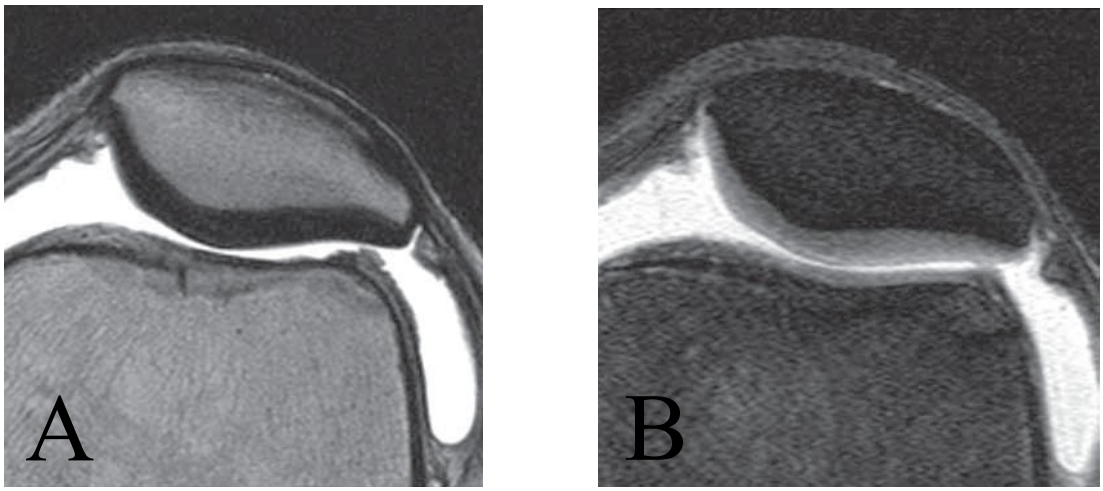

Fig 3.22 : A) T2 weighted non fat supressed image showing diffuse low signal intensity within cartilage and good contrast between cartilage and synovial fluid and poor contrast between cartilage and cortical bone. B) Axial intermediate weighted fat supressed image shows good contrast between cartilage and synovial fluid and sub chondral bone.

THREE-DIMENSIONAL FAST SE IMAGING :

3D GRE sequences provide images with isotropic voxels that improve the accuracy of articular cartilage imaging, but not suitable to image sub chondral bone [52,53]. 3D fast SE images on the other hand allows good depiction of articular cartilage and sub chondral marrow. In 3D fast SE imaging flip angle is modulated to reduce blurring and image acquisition time is shortened by parallel imaging.

3D SPGR IMAGING :

3D SPGR imaging is more sensitive than 2D sequences in morphological evaluation of articular cartilage. This sequence is also used in knee OA trials, in which a segmentation method is used in quantitative assessment of articular cartilage and is useful in detection of risk factors for progression of disease [54,55]. Small lesions can be obscured because of poor contrast between cartilage and fluid. This technique has low sensitivity for detecting lesions in areas other than cartilage because of magic angle effect. Long acquisition times and susceptibility artefacts are also the drawbacks in this sequence.

An SPGR-type technique called Fast low-angle shot (FLASH) imaging which uses a random gradient pulse to produce a phase shift and spoil the steady state is used for assessing change in cartilage thickness and volume over time in knee osteoarthritis trials [56] and assessment after chondrocyte implantation [57].

Fig 3.23 : Coronal 3D SPGR with lipid suppression image shows good contrast between cartilage and subchondral bone andhigh signal- intensity cartilaginous surfaces.

DEFT IMAGING :

3D driven equilibrium Fourier transform (DEFT) imaging is based on return of magnetization to z-axis after each excitation. The fluid and cartilage signal intensity is higher than that in SPGR and T2-weighted fast SE imaging respectively because of short T2 [58]. Fat is suppressed by the use of fat saturation pulse.

Motion artifacts, long acquisition times, incomplete fat saturation and poor sensitivity to sub chondral marrow edema make DEFT unsuitable for knee OA trials.

DESS IMAGING :

3D dual-echo steady state (DESS) uses two or more gradient echoes, with each group of two echoes separated by a refocusing pulse and the data from both echoes is used to obtain a higher T2* weighting for high signal intensity in cartilage and good contrast between cartilage and synovial fluid is obtained by increasing the flip angle that helps in detecting small sub chondral lesions [59]. Advantages of DESS imaging include short acquisition time, high SNR, high contrast between cartilage and fluid. One drawback is reduced sensitivity to alterations in internal cartilage intensity. Good accuracy and precision were noted in assessment of cartilage thickness and volume in knee OA trials [60].

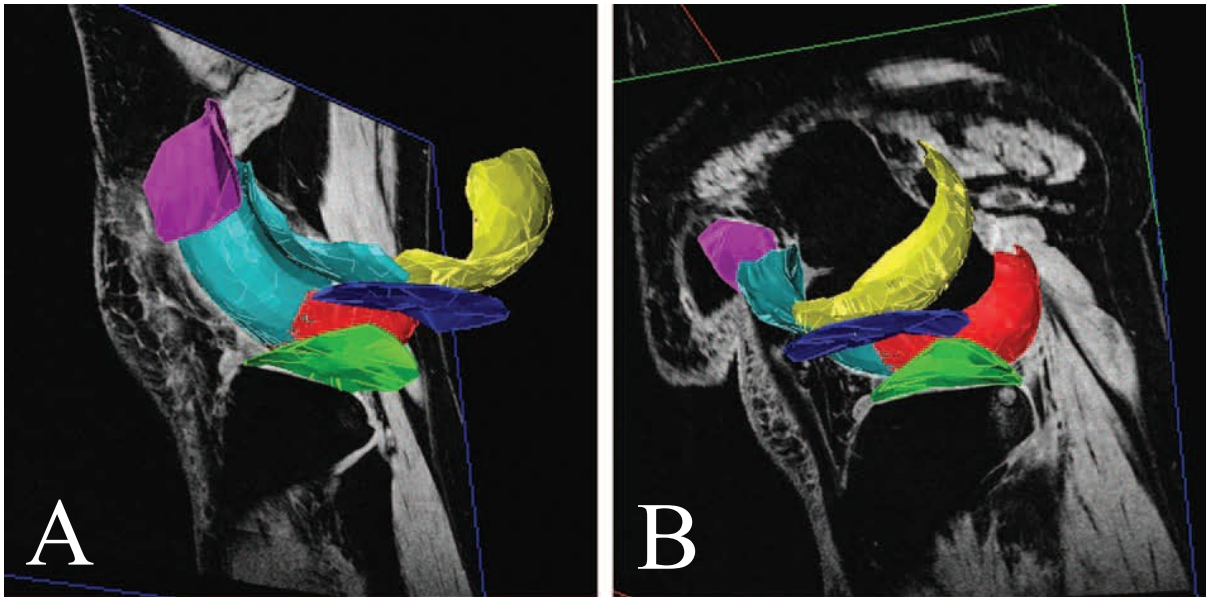

Fig 3.24 : Quantitation of cartilage in weight-bearing regions of the knee in different planes (A and B) using segmented sagittal 3D DESS image data.

[Red and yellow - femoral condyles, Dark blue and green - tibial plateaus, Light blue - trochlea, and Pink - patella.]

bSSFP IMAGING / TRUE FISP / FIESTA / BALANCED FFE IMAGING :

In 3D balanced steady state free precession (bSSFP) also known as true FISP (fast imaging with steady-state precession) or FIESTA (fast imaging employing steady-state acquisition) or balanced FFE (fast field echo), fluid is depicted as high signal intensity and signal intensity of cartilage is preserved, thus resulting in a good contrast between cartilage and synovial fluid. Fluctuating equilibrium MR (FEMR) imaging is a variant of bSSFP imaging and is used in the morphologic assessment of knee cartilage [(61)]. This technique produces 3D images within a short acquisition time [(62)].

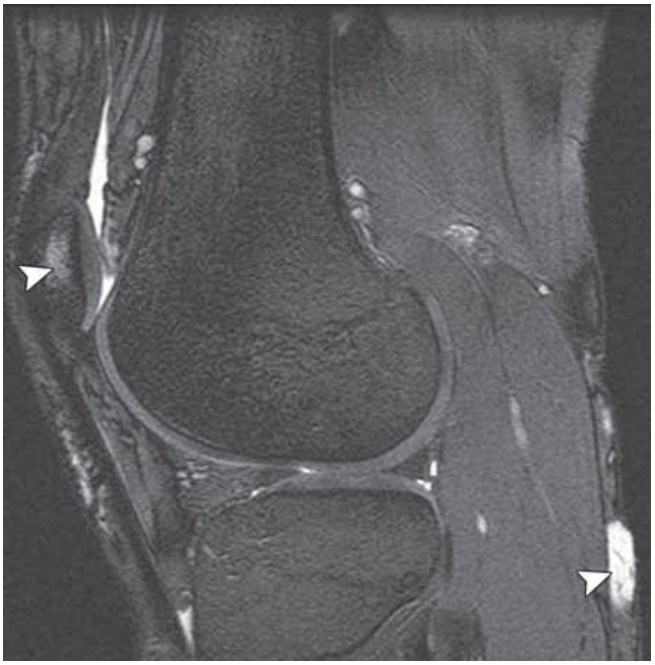

Fig 3.25 : Sagittal 3D bSSFP image obtained with a fluctuating equilibrium technique shows excellent contrast between cartilage and fluid. Arrowheads shows areas of imperfect fat-water separation due to field inhomogeneity.

SPACE IMAGING :

3D Fast SE sampling perfection with application-optimized contrast using different flip-angle evolutions (SPACE) is a technique in which a restore pulse is used to generate large turbo factors and a pseudo steady state is produced by varying flip angles. High T2 weighted tissue contrast and isotropic spatial resolutions are some of the advantages of this technique and has a better SNR efficiency compared to other 3D techniques [(63)]. The main disadvantage of this technique is its long acquisition time, which makes it less suitable for use in clinical trials.

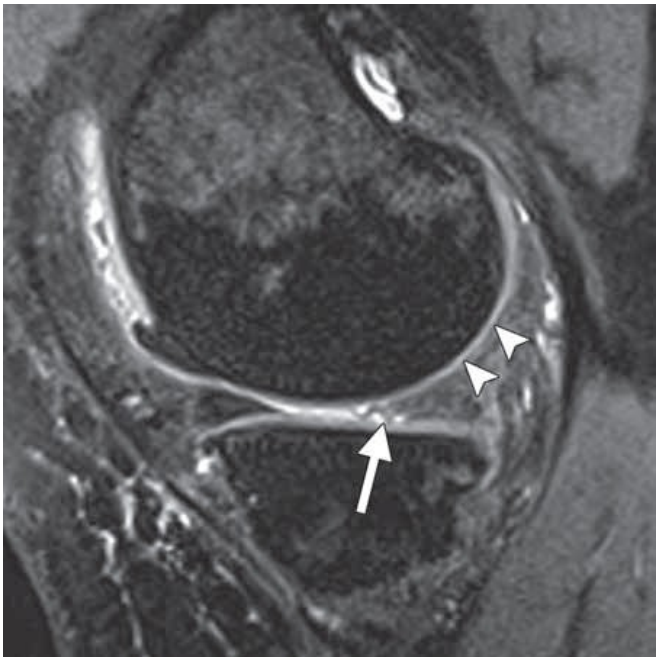

Fig 3.26 : 3D SPACE sagittal section shows medial femoral condyle cartilage thinning (arrowheads) and posterior horn of the medial meniscus tear (arrow).

COMPOSITIONAL IMAGING OF ARTICULAR CARTILAGE :

The mechanical load of the knee joint is mainly supported by the hyaline articular cartilage. The composition of articular cartilage is ; 75% - Interstitial fluid (water) containing elecrolytes, 20% - Type - 2 Collagen and 5% - other macromolecules, mainly aggrecan which is a aggregating proteoglycan. Tensile strength is provided mainly by collagen which acts as a structural framework. The orderly arranged collagen fibres along with its water content cause magnetisation transfer.

The negative charge of glycosaminoglycans (GAGs) are imparted by their carboxyl and sulfate groups. Therefore charged particles like sodium (Na+) ions and gadolinium based contrast agents like gadolinium diethylenetriaminepentaacetic acid $(Gd\text{-}DTPA)^{2-}$ are distributed within the joint in relation to the proteoglycan concentration.

The earliest stage of cartilage degeneration is indicated by decrease in GAGs and increase in water content. As the collagen and proteoglycan associated GAGs are the major components that maintain the integrity of cartilage compositional imaging of articular cartilage is mainly focussed on the assessment of collagen and GAG content.

STRUCTURE OF CARTILAGE :

The bio physical structure of cartilage is different in bone interface and articular surface [64]. The most superficial layer of cartilage at the articular surface is known as lamina splendens, consisting of dense collagen fibres that decrease the shear stress and friction along with synovial fluid [65]. Next layer is the tangential or superficial layer in which the collagen fibrils are parallel to articular surface. The deeper zone is the transition zone, consisting of anisotropic orientation of collagen fibrils [66]. The next zone is the radial zone in which the fibrils are perpendicular to bone surface [67]. The last zone is the tidemark, where the cartilage is anchored to the sub chondral bone by the collagen.

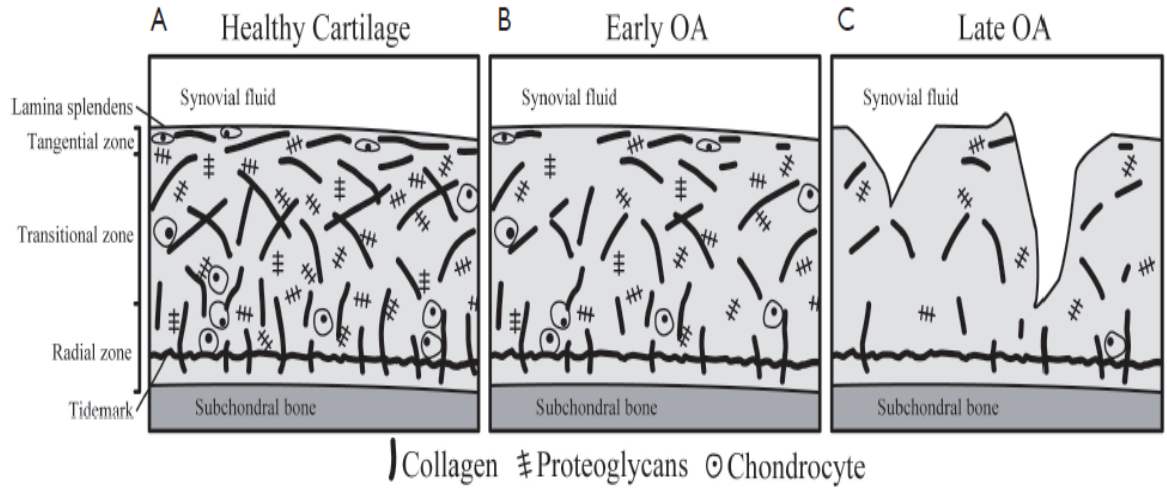

Fig 3.27 [68] : Articular cartilage composition at three stages of health. Healthy cartilage (A) demonstrates several distinct layers of collagen fibrils and abundant proteoglycans. Early stages of OA (B), showing depletion of proteoglycans, and break down of collagen matrix. Later stages of OA (C), severe depletion of proteoglycans and compromise of morphological structure.

The distribution of the cartilage layers is variable, according to the type of stress. Thicker radial zones and uniform collagen orientation are seen in weight bearing regions [69]. Transitional zone is thicker in periphery to resist strong shear forces [70].

The various methods of compositional assessment of articular cartilage are ;

- T2 mapping
- Delayed gadolinium-enhanced MR imaging of cartilage (or dGEMRIC)
- T1 ρ mapping
- Sodium imaging
- Diffusion weighted imaging

T2 MAPPING :

T2 refers to the relaxation time which is related to the speed at which nuclei lose phase coherence following excitation [71]. The loss of coherence results in decay of transverse magnetization vector and MR signal. Free water molecules slow down the loss of transverse magnetization thereby decreasing the rate of decay and increasing T2. As already stated earlier, the earliest stage of cartilage degeneration is indicated by decrease in GAGs and increase in water content. T2 mapping uses this relationship between T2 relaxation time and free water and serves as a tool for the indirect assessment of collagen content and orientation, which are important indicators

for early OA. T2 is highly sensitive to alterations in water content and collagen concentration [72]. Varying T2 in a normal cartilage is due to zonal and regional differences in collagen matrix organisation. T2 values are measured by a multi echo SE sequence. Routine MR sequences provide only a subjective assessment of articular cartilage. T2 mapping allows objective assessment of cartilage, which is done through the colour or grey scale maps generated by it. With the help of these maps variations in T2 within the articular cartilage can be identified. The early detection of cartilage degeneration by this technique is used in monitoring treatment of OA and in evaluation of cartilage post surgery.

In a healthy cartilage the collagen and proteoglycan matrix traps the water protons and make them less mobile, so there is low signal intensity on T2-weighted images. In the earliest stages of OA, the breakdown of collagen, proteoglycan and GAG matrix renders the articular cartilage more permeable to water, leading to an elevation in T2 relaxation times.

T2 values are higher and more heterogenous in sites of early cartilage degeneration, which signifies areas of early disruption of collagen matrix than in normal cartilage [5,8]. But the increase in T2 does not have a linear relationship with severity of the disease [73] and variations in T2 can also be seen between tibial and femoral cartilages [8]. Cartilage T2 values can also be affected by physical exercises [74].

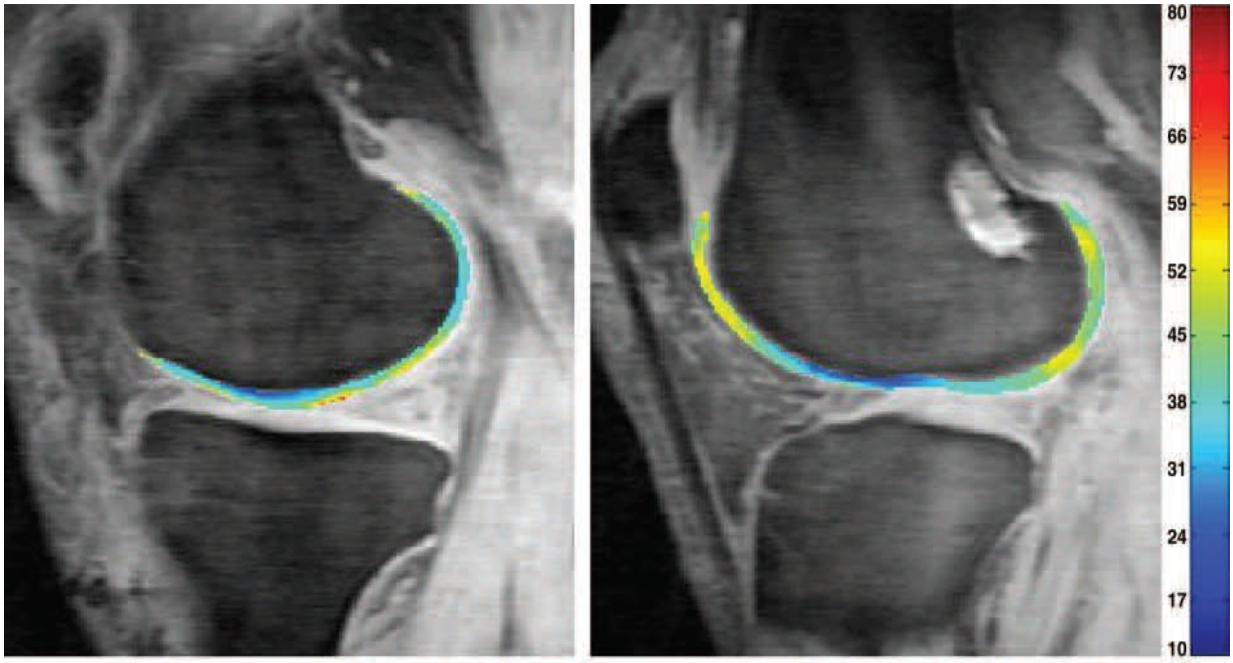

Fig 3.28 : Sagittal T2 map shows higher T2 values (yellow) in the medial (a) and lateral (b) tibiofemoral compartments, suggestive of deterioration of the integrity and orientation of the collagen network.

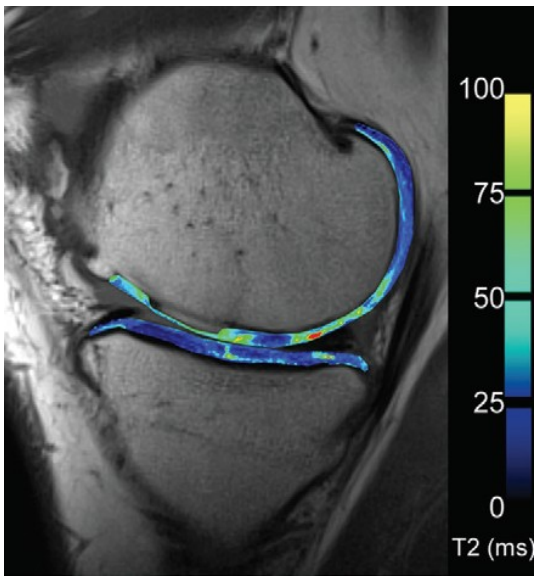

Fig 3.29 :Sagittal T2 map shows areas of increased T2 values in femoral medial condyle.

Dark blue = low T2 values, light blue and yellow = higher T2 values.

The normal articular cartilage has a lower T2 value in deep layer than the superficial layer. The deep layer on the medial and lateral femoral condyles and medial and lateral tibial plateaus and patella have a T2 value between 20 to 30 msec. The superficial layer in these areas have a higher T2 value between 40 to 50 msec [75].

OTHER METHODS OF COMPOSITIONAL IMAGING OF CARTILAGE : dGEMRIC TECHNIQUE : (DELAYED GADOLINIUM-ENHANCED MR IMAGING OF CARTILAGE)

Gadolinium based contrast agents like gadolinium diethylenetriamine pentaacetic acid $(Gd\text{-}DTPA)^{2-}$ have a negative charge and are distributed within the joint in relation to the proteoglycan concentration, which in turn also have a negative charge imparted by the carboxyl and sulfate groups of GAGs. Therefore $(Gd\text{-}DTPA)^{2-}$ will concentrate in areas of low GAG concentration. $(Gd\text{-}DTPA)^{2-}$ is highly paramagnetic and causes relaxation of adjacent protons following a radiofrequency (RF) pulse, resulting in a decreased T1 value in areas with high levels of $(Gd\text{-}DTPA)^{2-}$. Therefore, T1 is used as the quantitative measure in this technique. Lower T1 indicates reduced GAG concentration.

Following intra venous administration of contrast, limb is moved for 10 minutes to facilitate distribution of contrast within the joint. T1 values are measured 90 minutes after contrast injection by 3D SPGR sequence [76]. The resulting T1 value is known as dGEMRIC index. Lower dGEMRIC index is seen in OA [77]. The

dGEMRIC index can be affected by factors like exercise and body mass index [78,79,]. This non invasive technique can be used for monitoring the GAG content of cartilage post surgery [80,81] and detect cartilage changes that can progress to OA [82].

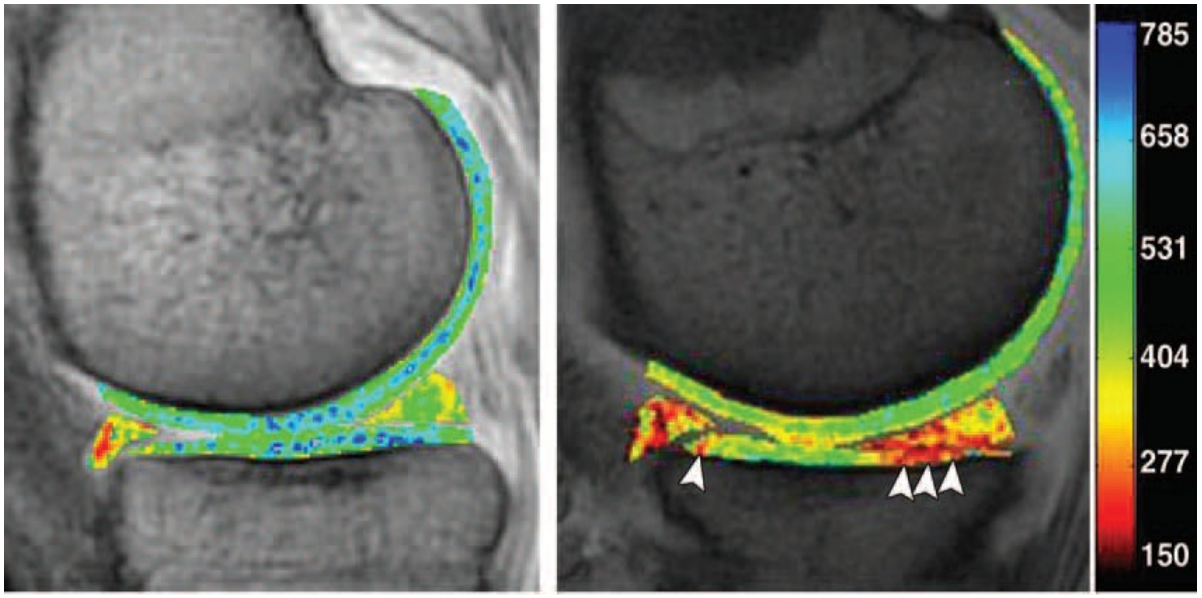

Fig 3.30 : dGEMRIC index in a patient with osteoarthritis (b) shows lower index values than a normal subject (a) indicating depletion of the GAG content in medial tibial plateau (arrowheads)

The disadvantages of this technique are requirement of intra venous contrast administration and delay time taken for the contrast to distribute within the joint cavity.

T1 ρ MAPPING :

Changes in OA like depletion of proteoglycans can alter T1 ρ values, as T1 ρ values can be altered by the interactions between the water molecules and extra cellular matrix. Increased T1 ρ values are seen in cartilage affected by OA. Despite its higher sensitivity than T2 weighted imaging [84] T1 ρ mapping is not suitable for large clinical trials, because of its time consuming nature and requirement of special sequences which are not available widely.

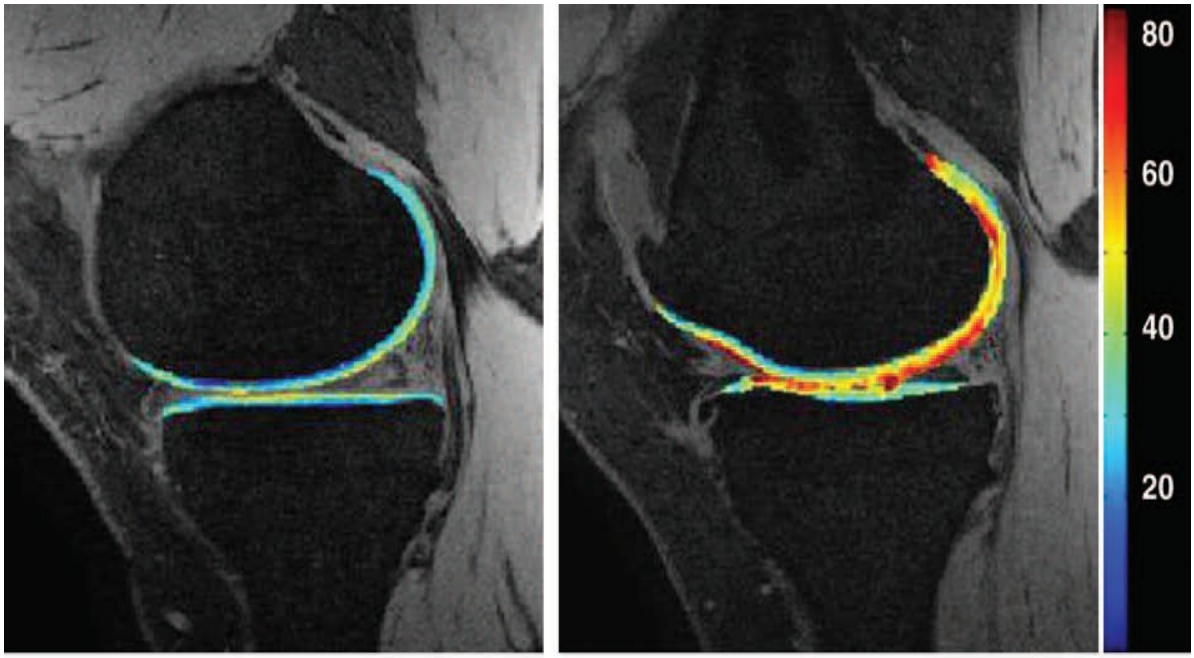

Fig 3.31 : T1 ρ mapping images in a patient with osteoarthritis (b) shows higher T1 ρ values than a normal subject (a).

SODIUM IMAGING :

Positively charged Sodium cations are attracted to negatively charged GAGs and are distributed in accordance with GAG content. Thus this technique can be used as an indirect method of assessing GAG concentration. Cartilage with GAG depletion have lower concentrations of Na and therefore will have lower signal intensity than normal cartilage [84-86].

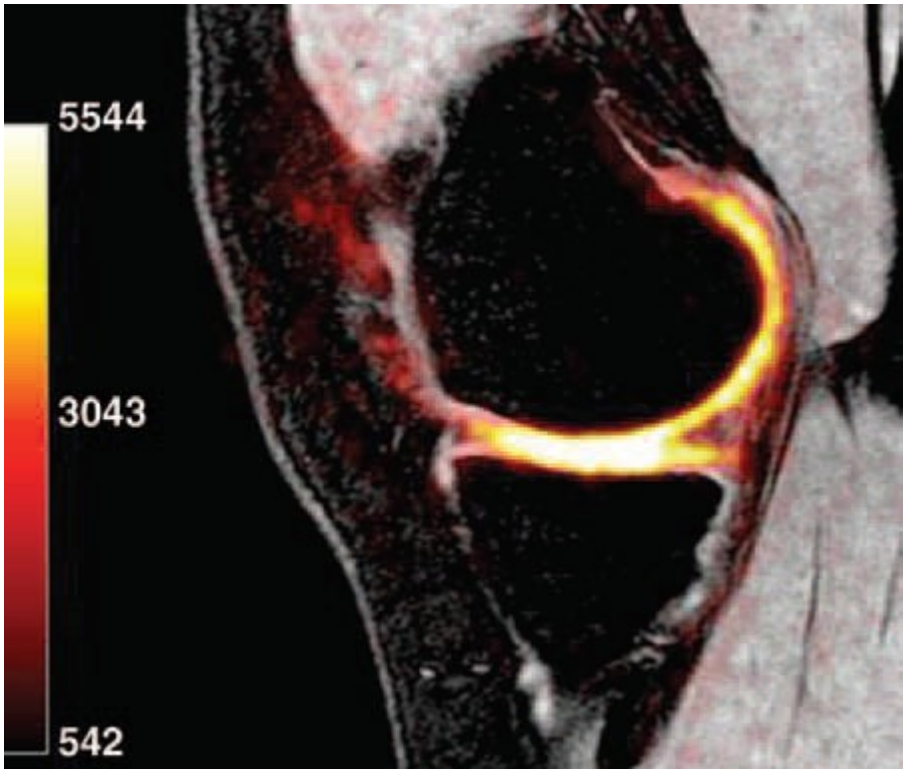

Fig 3.32 : PD–weighted SPGR sequence sodium MR image obtained with a quadrature sodium coil in a normal 20-year-old shows high signal intensity in cartilage at the medial compartment.

PREVIOUS STUDIES ON T2 MAPPING :

A review of the literature revealed several publications using T2 mapping, in which OA was studied along with various other sequences for compositional assessment of articular cartilage.

X. Li et al. and C. Benjamin et al. [87] did T2 and T1 ρ mapping of articular cartilage in OA knee using a 3T MRI. Both in vivo T2 and T1 ρ relaxation times increased with the degree of cartilage degeneration. T1 ρ relaxation time was a more sensitive indicator for early cartilage degeneration than T2.

Liess C et al., Lüsse S et al., Karger N et al., Heller M et al., and Glüer CC et al. [72] detected the changes in cartilage water content using in vivo T2-mapping, following knee bends and after 45 minutes of rest. Both cartilage thickness and T2 values increased following 45 minutes of rest.

M. Runge et al. and Besançon et al. [88] evaluated the efficiency of T2 mapping to detect cartilage degeneration. Some patients had a pathological T2 map with a focal increased T2 value and in some patients who had normal T2 values, T2 map visualized a defect in the superficial, middle and deep
zones of the patellar cartilage

Richard Kijowski, MD et al. ; Donna G. Blankenbaker MD et al. ; Alejandro Munoz del Rio, PhD et al. ; Geoffrey S. Baer, MD et al. and Ben K. Graf, MD et al. [75] evaluated the value of Adding a T2 Mapping Sequence to a Routine MR Imaging Protocol in 3T. Addition of a T2 mapping sequence improved sensitivity in the detection of cartilage lesions within the knee joint from 74.6% to 88.9%, with only a small reduction in specificity.

Hannila et al. [89] compared T2 mapping sequence with a routine MR imaging protocol and evaluated patellar cartilage and found that eight areas of increased T2 relaxation time corresponded to normal-appearing cartilage identified by using the routine MR protocol.

Apprich et al. [90] evaluated the articular cartilage of the medial femoral condyle in 43 patients at 3.0 T by using a T2 mapping sequence and found a significant association between the T2 relaxation time and the morphologic grade of the cartilage lesion.

Regatte RR et al. , Akella SV et al. [91] studied the proteoglycan depletion-induced changes in transverse relaxation maps of cartilage and compared T2 and T1rho maps. Unchanged or decreased T2 relaxation time with in vitro cartilage degeneration was reported.

4. AIM OF THE STUDY

PRIMARY OBJECTIVES :

1. To determine the ability of MR T2 mapping to detect cartilage matrix degeneration in OA patients.
2. To compare the T2 relaxation values in normal subjects and cartilage patients with OA.

SECONDARY OBJECTIVES :

1. To compare the cartilage thickness in normal subjects and cartilage patients with OA.
2. To study the relationship between Kellgren - Lawrence scores based on plain radiographs and the T2 values in cartilage with OA.

5. MATERIALS AND METHODS

5.1 Study Area : Barnard Institute of Radiology,
Madras Medical College, Chennai.

5.2 Study Period : 6 months (June 2017 – December 2017)

5.3 Sample Size **:** 40

5.4 Study Design : Prospective study

5. 5 Inclusion criteria :

- Patients with clinical osteoarthritis symptoms and radiological findings who are referred for MRI
- Patients refered to MRI for other clinical symptoms besides osteoarthritis

5. 6 Exclusion criteria :

- Patients with orthopnea, claustrophobia
- Patients with MRI non-compatible implants

5.7 METHODOLOGY :

This prospective study was performed after obtaining clearance from our Institutional Ethics Committee and institutional informed consent guidelines were observed.

5.7.1 STUDY POPULATION :

Patients referred from orthopaedics department with symptoms of OA, diagnosed clinically and radiologically by x – ray and patients without clinical or radiological evidence of OA who were referred for MRI knee for purposes, who were willing for cartilage mapping were included in this study during the period from June to December 2017.

The patients were screened using the drawn inclusion/ exclusion criteria. Relevant entries in the proforma for each patient were made after reviewing his/her case sheet & previous medical records. The final population enrolled in this study composed of 40 patients, of which 15 patients had clinical and radiological evidence of OA and 25 patients didn't have clinical or radiological evidence of OA and served as controls.

5.7.2 IMAGING PROTOCOL :

In all the patients, two standard radiographic views were taken as follows: Bilateral standing flexion weight bearing view and 30^0 flexion lateral view.

All MR T2 mapping studies were performed in a 3 Tesla MRI scanner (MAGNETOM SKYRA, SIEMENS HEALTHINEERS) using a 15 channel knee coil and the images were acquired with 3 mm slice thickness. The sequences included in the protocol are as follows : sagittal T1 weighted SE imaging (time of repetition (TR)/time of echo (TE) 575/9.1 ms, field of view (FOV) : 140 mm, matrix : 256 x 256, number of excitations [NEX] : 1), sagittal and axial fat supressed (FS) proton density (PD) SE imaging (TR/TE : 3600/25 ms), sagittal PD space (TR/TE : 1200/28 ms, FOV : 160, NEX : 1), Short tau inversion recovery (STIR) coronal (TR/TE : 5000/25 ms, FOV : 160, NEX : 2), axial, coronal and sagittal T2 anatomical (T2 mapping) sequence (TR/TE : 1000/14 ms, FOV : 160, NEX : 1). The T2 mapping sequence was taken covering the regions from top of the patellar cartilage to the femoro tibial cartilage. The acquisition time for the axial, coronal and sagittal T2 mapping sequence was ten minutes. The total duration of the study was twenty five minutes. .

5.7.3 IMAGE POST PROCESSING AND ANALYSIS:

The x ray findings were scored according to the KL scale, which is a standard OA grading system. The presence of joint space narrowing, osteophytes at joint margins and sub chondral sclerosis were analysed.

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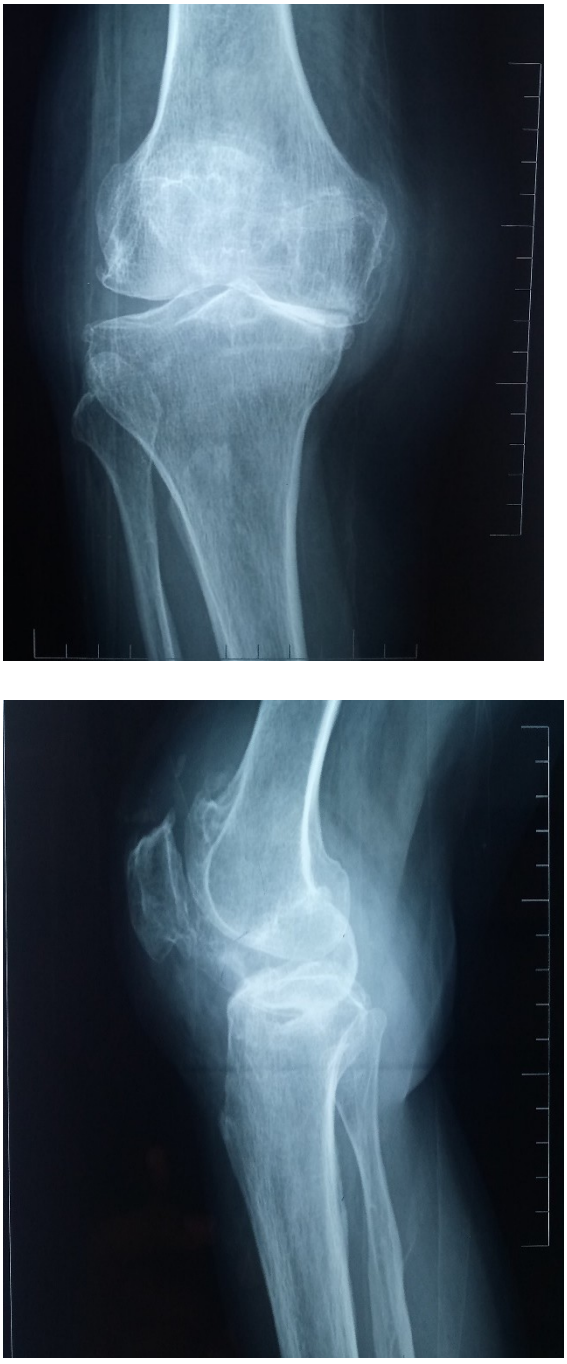
Five compartments were defined in each subject: patella (P), medial femoral condyle (MFC), lateral femoral condyle (LFC), medial tibia (MT) and lateral tibia (LT). The MR images were analysed regarding cartilage lesions, joint effusion, popliteal cysts, ligaments and menisci and features of OA like reactive bone marrow changes, osteophytes, subchondral cysts and loose bodies.

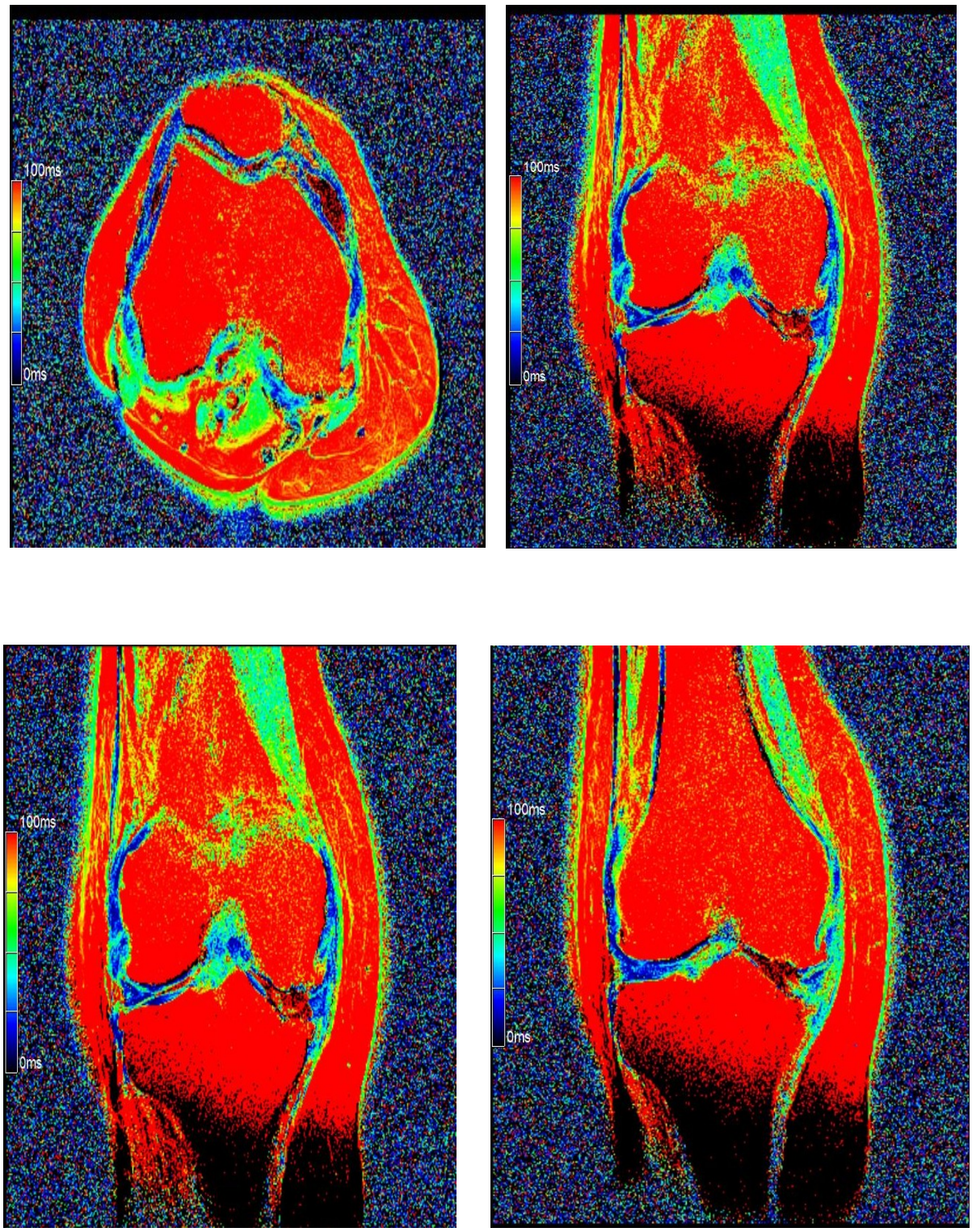
The MR images were transferred to a work station for off line quantification of T2 values and cartilage thickness in each of the five compartments. The average thickness was calculated for each slice and then averaged for all the slices. Similarly, the average T2 value was calculated by means of elliptical region of interest (ROI) for each slice and then averaged for all the slices in each of the five compartments.

CASE 1

History : 68 years old female, with right knee pain and swelling for 15 years.



X ray knee joint AP and lateral view showing severe medial joint space narrowing, multiple osteophytes and bony deformity – KL score – 4.



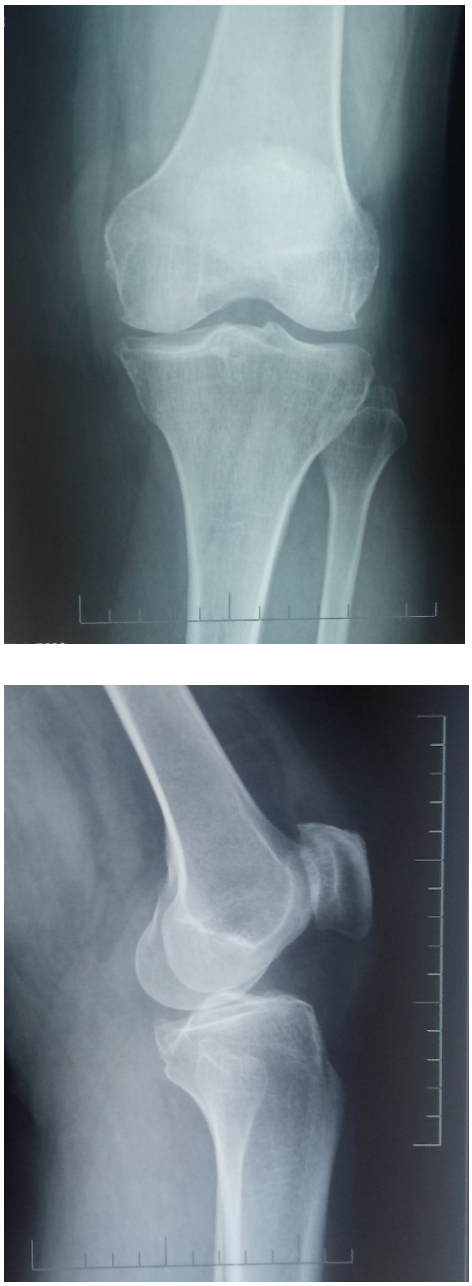
Axial and coronal T2 mapping images shows increased T2 values indicated by colour scale in medial patello femoral cartilage and increased T2 values and complete loss of cartilage in medial femoral condyle and medial tibial plateau.

REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC	**52.2**	**0.8**	**4**
LFC	**42**	**1.9**	
MT	**51.3**	**1.2**	
LT	**45.8**	**2.1**	
PATELLA	**39.5**	**2.4**	

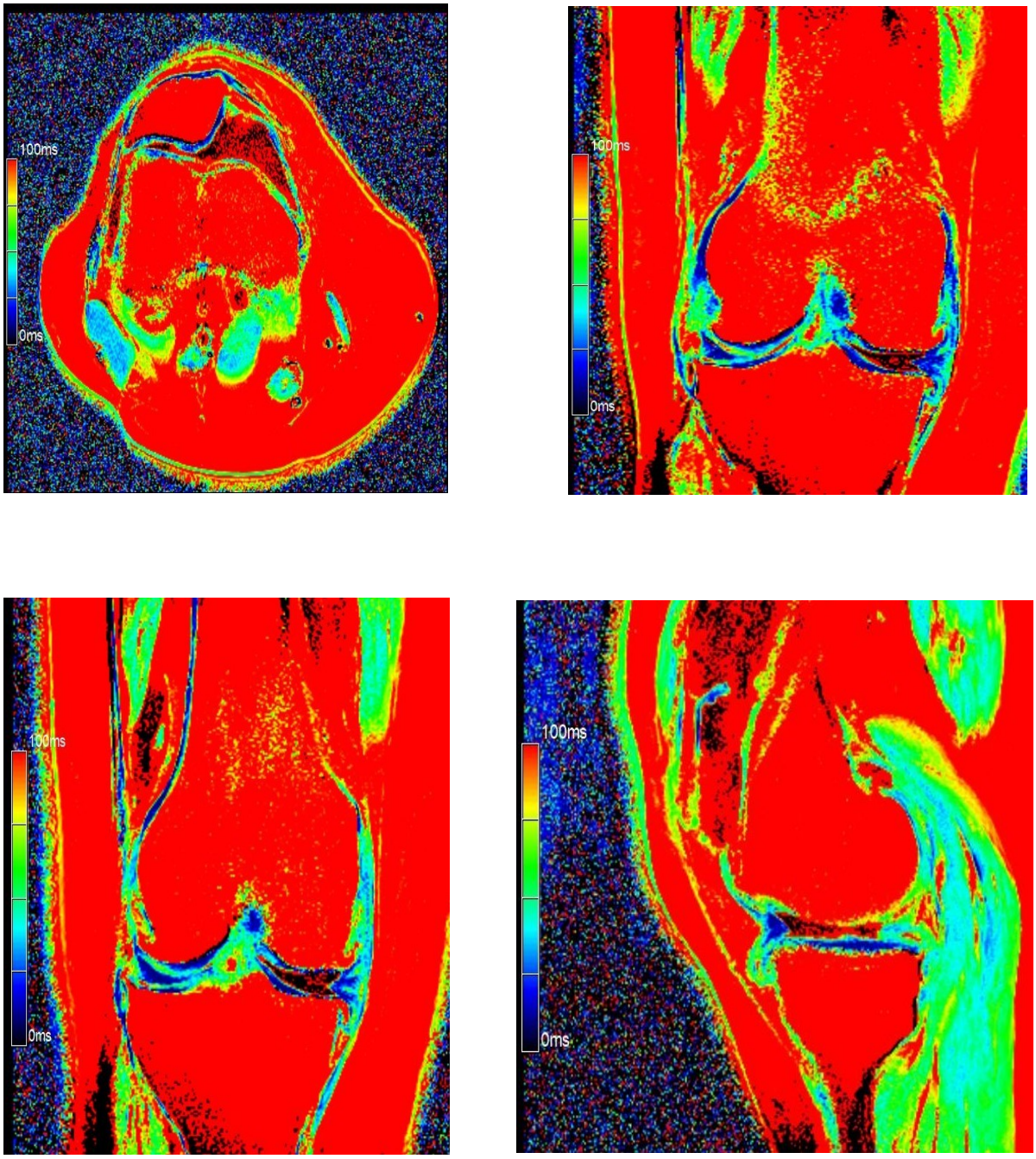
Overall Average T2 value : 46.16

CASE 2

History : 54 years old female, with right knee pain & difficulty in walking for 2 years.



X ray knee joint AP and lateral view shows medial joint space narrowing, multiple osteophytes and sub chondral sclerosis – KL score – 3.



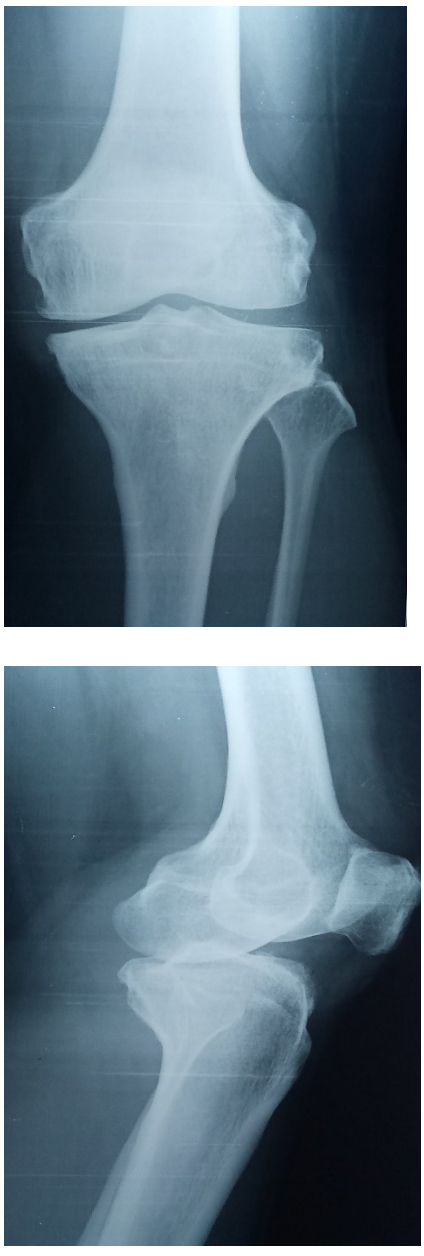
Axial, coronal and sagittal T2 mapping images shows increased T2 values indicated by colour scale and significant thinning and focal loss of cartilage in medial femoral condyle and medial tibial plateau.

REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC	**40.2**	**1.3**	**3**
LFC	**38.5**	**2.5**	
MT	**42.6**	**1.6**	
LT	**39.2**	**2**	
PATELLA	**37**	**1.8**	

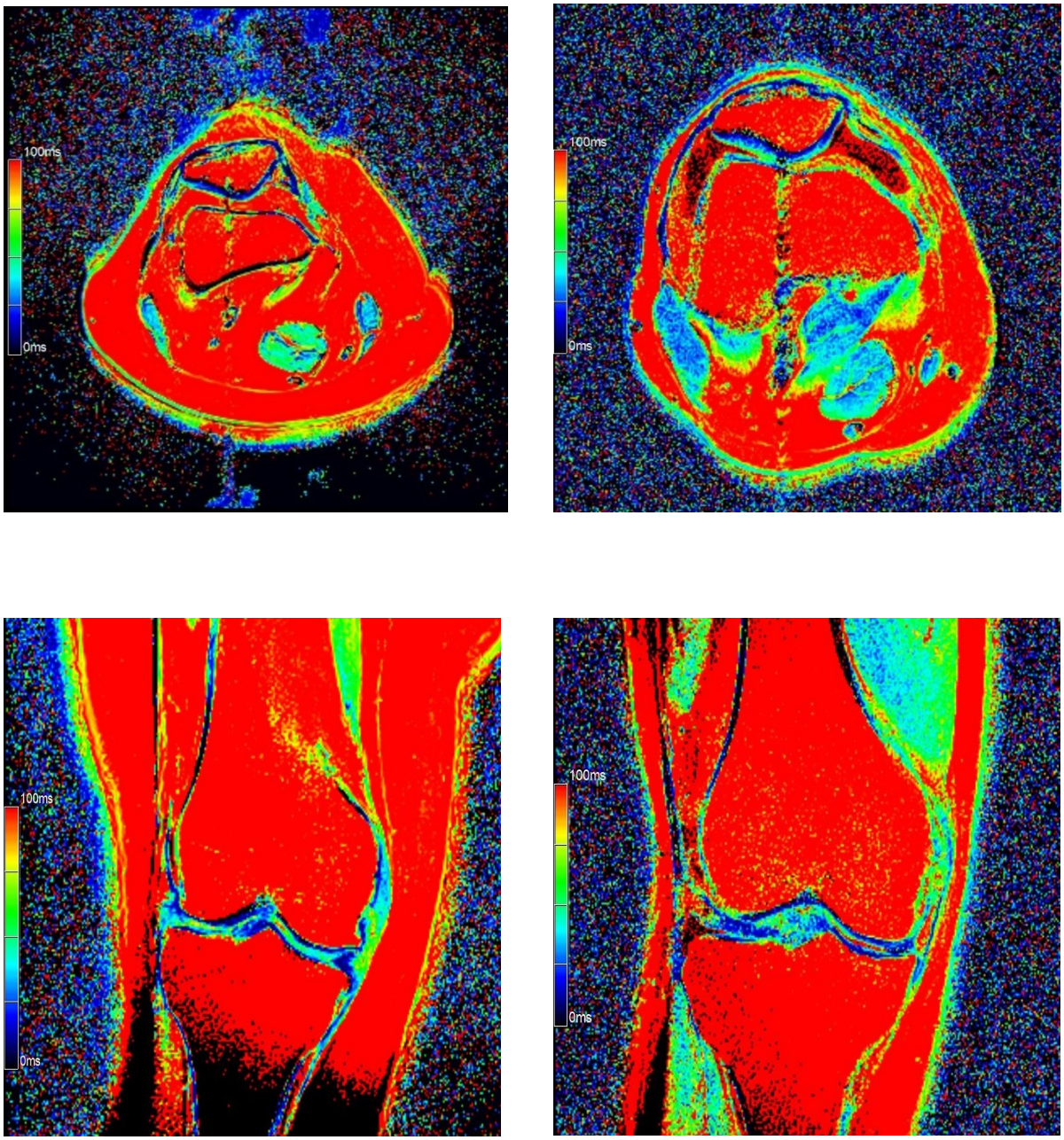
Overall Average T2 value : 39.5

CASE 3

History : 50 years old female, with right knee pain & difficulty in walking for 1 year.



X ray knee joint AP and lateral view shows few possible osteophytic lipping in medial & lateral femoral and tibial condyles and doubtful medial joint space narrowing – KL score – 1.



Axial and coronal T2 mapping images shows focal increase in T2 values in lateral tibial plateau. No evidence of significant cartilage loss. No evidence of increased T2 values in medial and lateral femoral condyles.

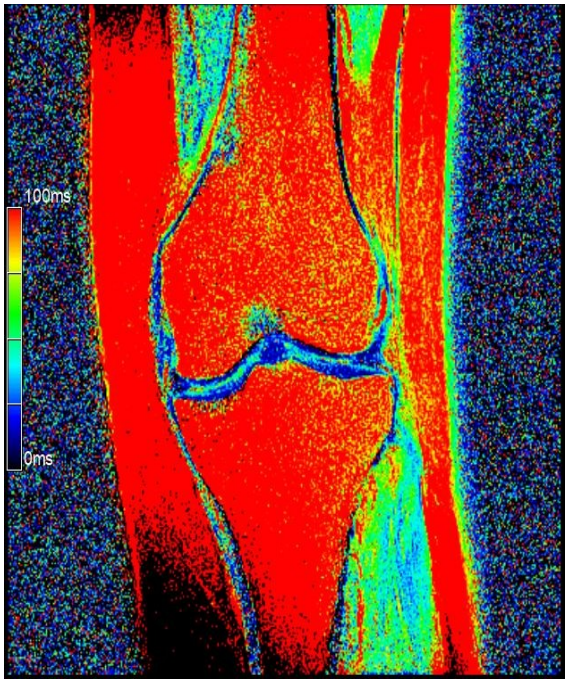
REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC	**29.4**	**1**	**1**
LFC	**22.1**	**1.5**	
MT	**31.5**	**1.2**	
LT	**32.1**	**1.1**	
PATELLA	**26.1**	**1.7**	

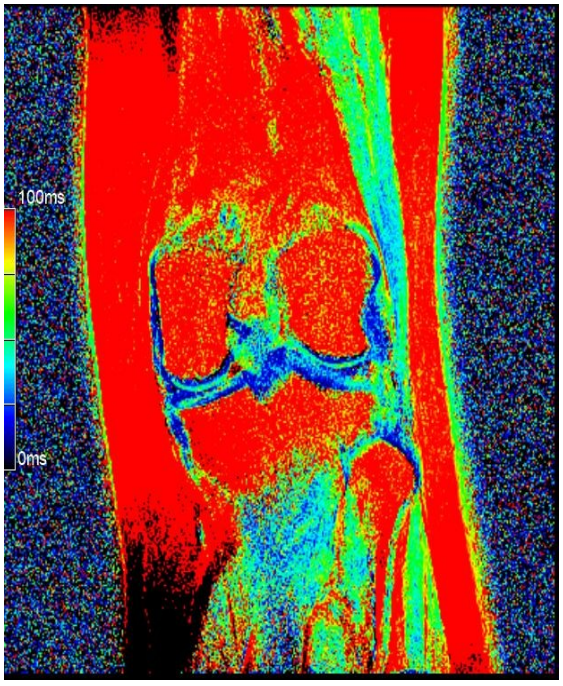
Overall Average T2 value : 28.2

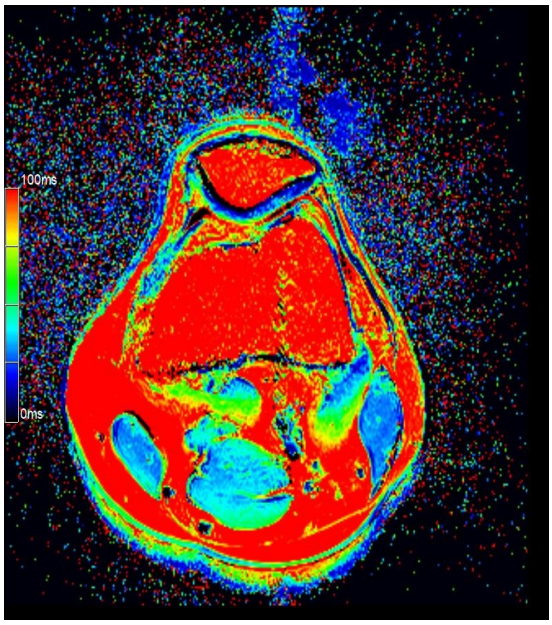
CASE 4

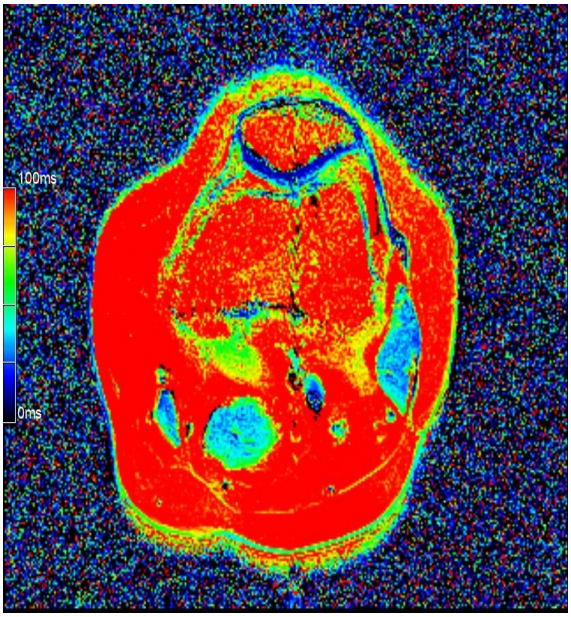
History : 29 years old female, with left knee pain following a fall on the ground. No clinical signs of OA.

X ray knee joint AP and lateral view shows no evidence of joint space narrowing or osteophytes – KL score - 0









Axial and coronal T2 mapping images shows no evidence of significant cartilage loss. No evidence of increased T2 values noted in medial and lateral femoral and tibial condyles and in patella.

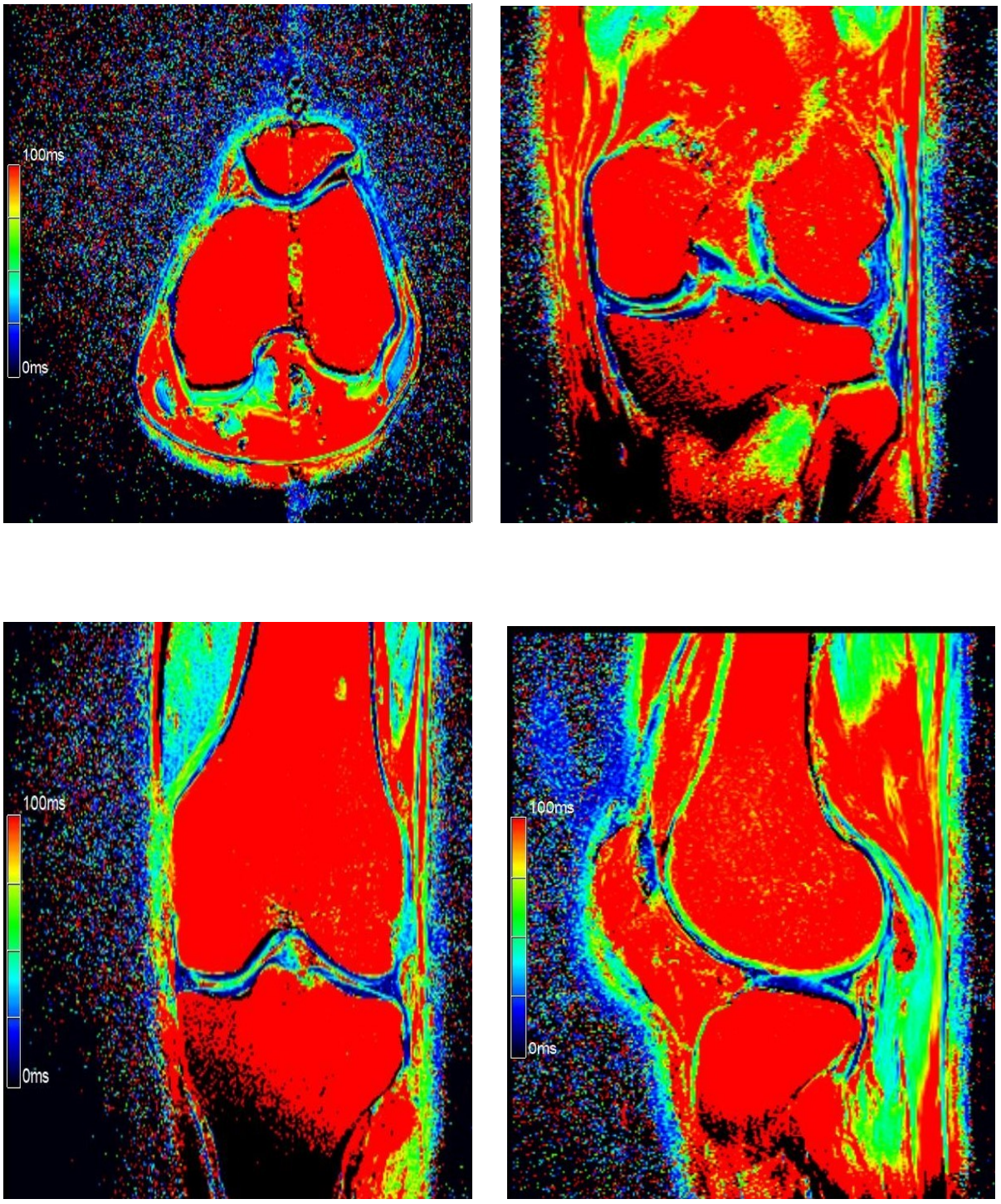
REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC	**28.5**	**1.9**	**0**
LFC	**26.3**	**1.7**	
MT	**28.6**	**2.7**	
LT	**29.5**	**2.8**	
PATELLA	**31.3**	**2.6**	

Overall Average T2 value : 28.8

CASE 5

History : 32 years old male, with left knee pain following a road traffic accident. No clinical signs of OA.

X ray knee joint AP and lateral view shows no evidence of joint space narrowing or osteophytes – KL score - 0



Axial, coronal and sagittal T2 mapping images shows no evidence of significant cartilage loss. No evidence of increased T2 values noted in medial and lateral femoral and tibial condyles and in patella.

REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC	**25.5**	**1.2**	**0**
LFC	**28**	**2.8**	
MT	**29.3**	**3**	
LT	**25.6**	**2.6**	
PATELLA	**27**	**3.1**	

Overall Average T2 value : 27.08

6. STATISTICAL ANALYSIS

The collected data from all the enrolled patients were analysed with IBM.SPSS statistics software 23.0 Version.

To describe about the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & Standard Deviation were used for continuous variables.

To find the significant difference between the bivariate samples in the independent groups, the unpaired sample t-test was used.

To find the significance in categorical data Chi-Square test was used.

In both the above statistical tools the probability value .05 is considered as significant level.

7. OBSERVATION AND RESULTS

7.1 AGE RANGE DISTRIBUTION :

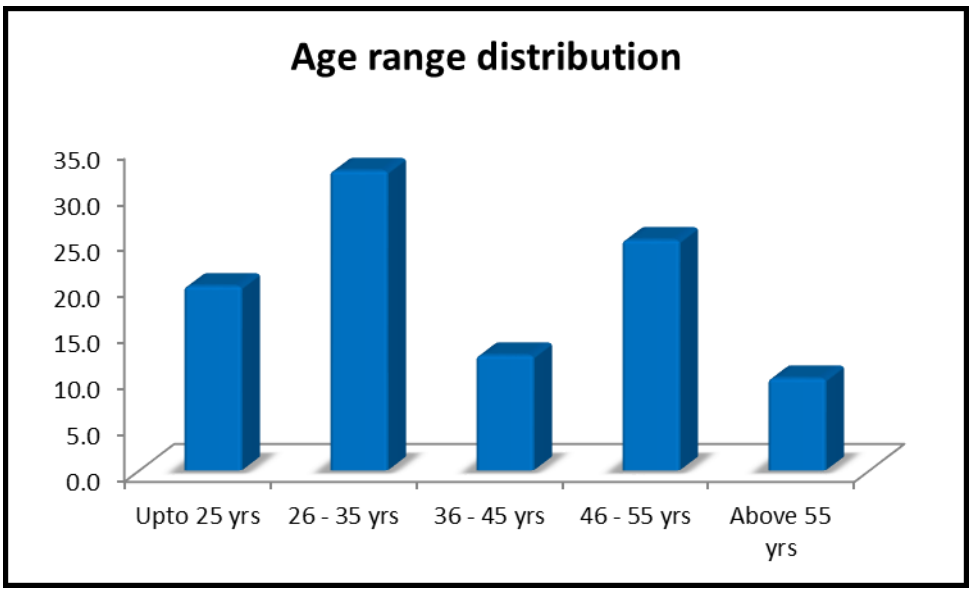


Fig: 7.1.1 : Bar diagram showing the age range distribution of the study group.

Age range

		Frequency	Percent
Valid	Upto 25 yrs	8	20.0
	26 - 35 yrs	13	32.5
	36 - 45 yrs	5	12.5
	46 - 55 yrs	10	25.0
	Above 55 yrs	4	10.0
	Total	40	100.0

Table : 7.1.1 : Frequency table showing the age range distribution of the study group. Average age of the participants in the study = 38±14 years.

7.2 GENDER DISTRIBUTION :

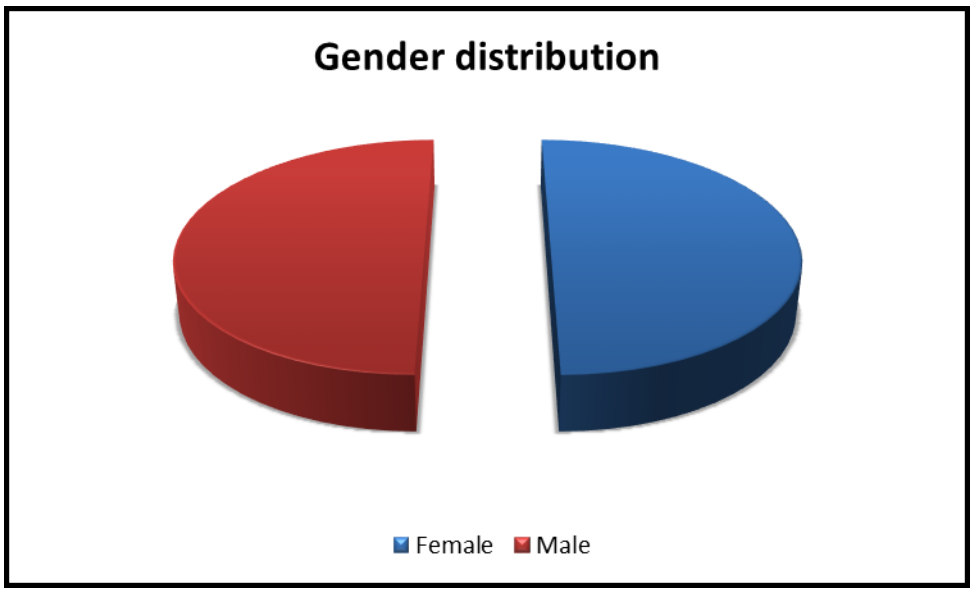


Fig: 7.2.1 : Pie chart showing the gender distribution among the study group.

SEX

		Frequency	Percent
Valid	Female	20	50.0
	Male	20	50.0
	Total	40	100.0

Table: 7.2.1 : Frequency table showing the gender distribution among the study group.

7.3 CROSS TABULATIONS – GENDER DISTRIBUTION IN TESTS AND CONTROLS :

Crosstab

			Groups		
			Test	Control	Total
SEX	F	Count	10	10	20
		% within Groups	66.7%	40.0%	50.0%
	M	Count	5	15	20
		% within Groups	33.3%	60.0%	50.0%
Total		Count	15	25	40
		% within Groups	100.0%	100.0%	100.0%

Table: 7.3.1 : Cross tabulation showing the gender distribution of the tests and controls among the study group.

SEX	TEST	CONTROL
MALE	66.7%	40%
FEMALE	33.3%	60%

Table: 7.3.2 : Frequency table showing the gender distribution among the tests and controls in the study group.

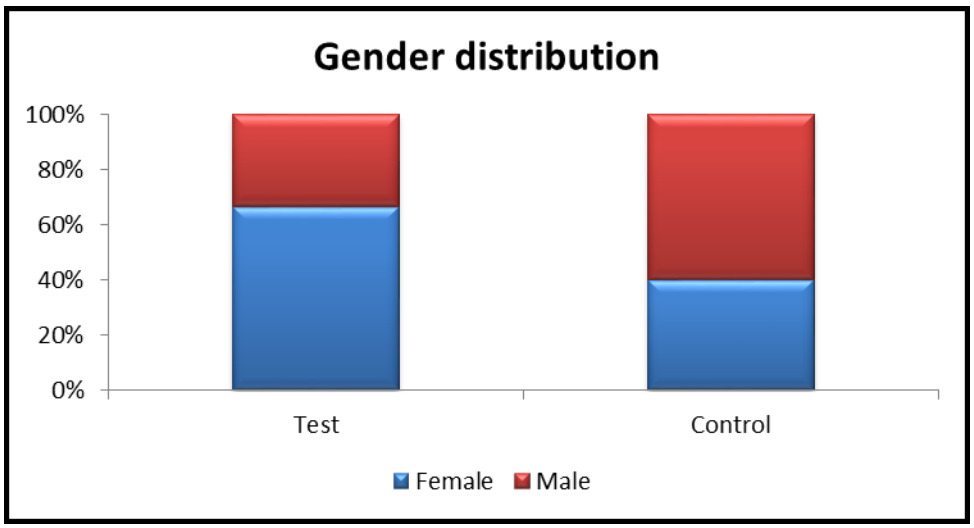


Fig: 7.3.1 : Bar diagram showing the gender distribution of the tests and controls among the study group.

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.667[a]	1	.102		
Continuity Correction[b]	1.707	1	.191		
Likelihood Ratio	2.706	1	.100		
Fisher's Exact Test				.191	.095
N of Valid Cases	40				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.50.
b. Computed only for a 2x2 table

Table 7.3.3 : Chi square test showing no significant difference (P=0.102) in gender distribution among the tests and controls in the study group.

7.4 COMPARISON OF KL SCORE BETWEEN TESTS AND CONTROLS :

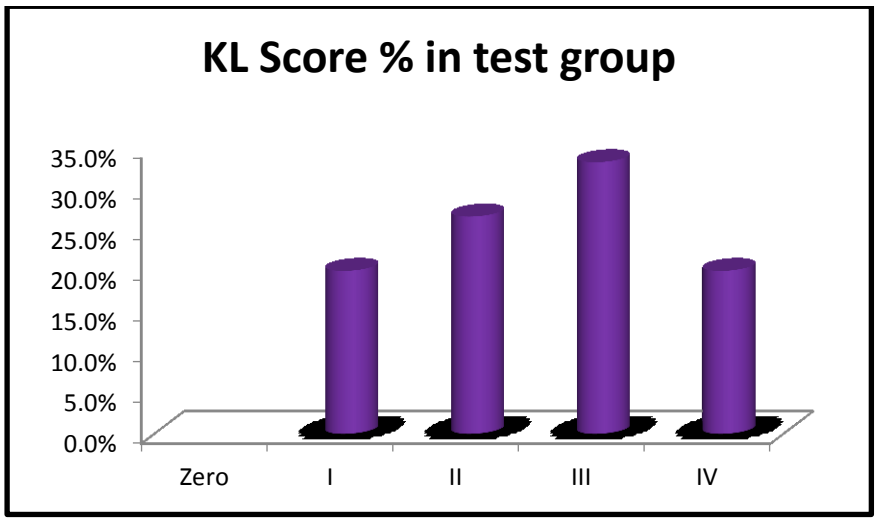


Fig 7.4.1 : Bar diagram showing KL scores distribution among the tests in the study group

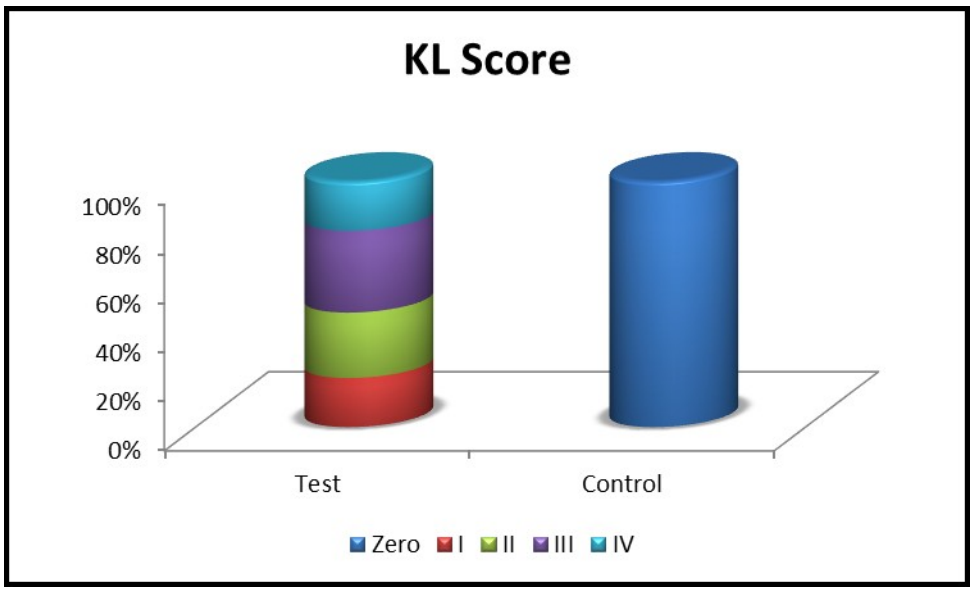


Fig 7.4.2 : Bar diagram showing KL scores distribution among the tests and controls in the study group.

Crosstab

			Groups		
			Test	Control	Total
KL SCORE	0	Count	0	25	25
		% within Groups	0.0%	100.0%	62.5%
	1	Count	3	0	3
		% within Groups	20.0%	0.0%	7.5%
	2	Count	4	0	4
		% within Groups	26.7%	0.0%	10.0%
	3	Count	5	0	5
		% within Groups	33.3%	0.0%	12.5%
	4	Count	3	0	3
		% within Groups	20.0%	0.0%	7.5%
Total		Count	15	25	40
		% within Groups	100.0%	100.0%	100.0%

Table 7.4.1 : Cross tabulation showing KL score distribution among the tests and controls in the study group

KL SCORE	TEST	CONTROL
0	0%	100%
1	20%	
2	26.7%	
3	33%	
4	20%	

Table 7.4.2 : Frequency table showing the KL score distribution among the tests and controls in the study group.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	40.000[a]	4	.0005
Likelihood Ratio	52.925	4	.000
Linear-by-Linear Association	30.916	1	.000
N of Valid Cases	40		

a. 8 cells (80.0%) have expected count less than 5. The minimum expected count is 1.13.

Table 7.4.3 Chi square test of the comparison of KL scores between tests and controls, which shows that there is a statistical significance (P = 0.0005).

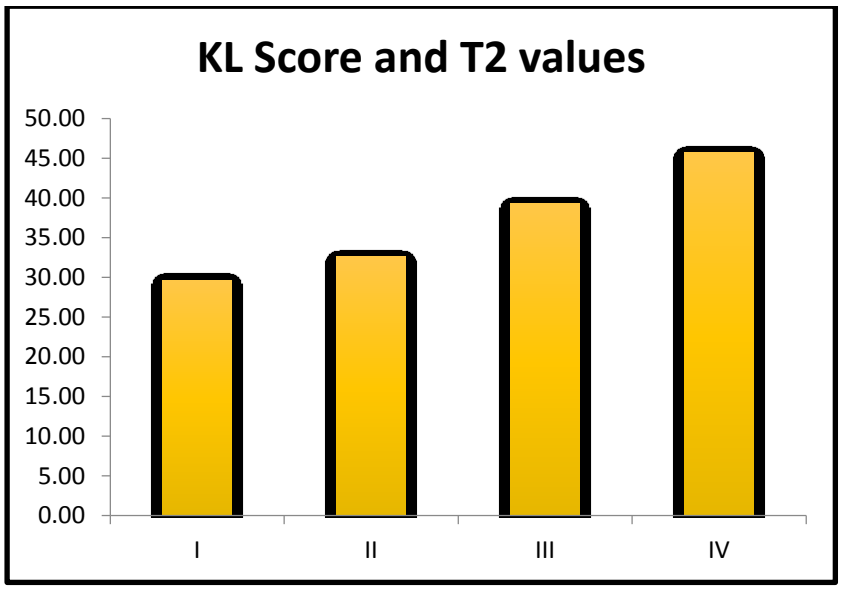
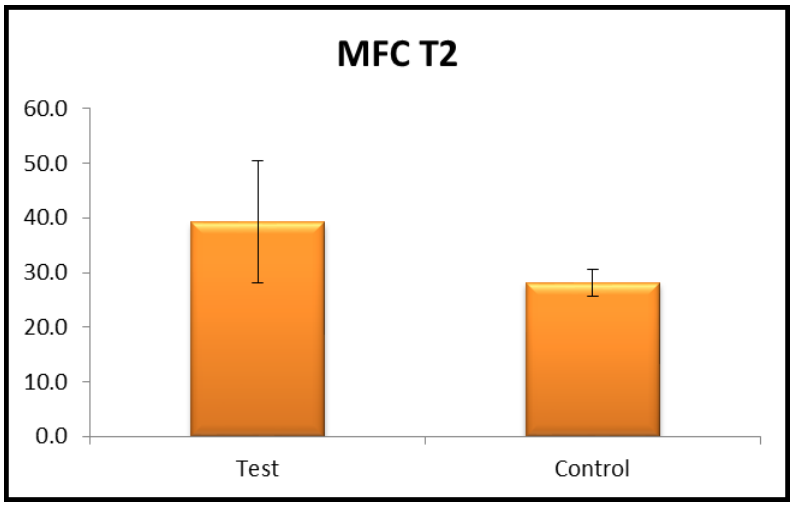


Fig 7.4.3 KL scores and T2 values : The average T2 values increased as KL scores increased based on x rays, with T2 values of 29.65, 32.58, 39.30 and 45.69 for KL scores 1,2,3 and 4 respectively.

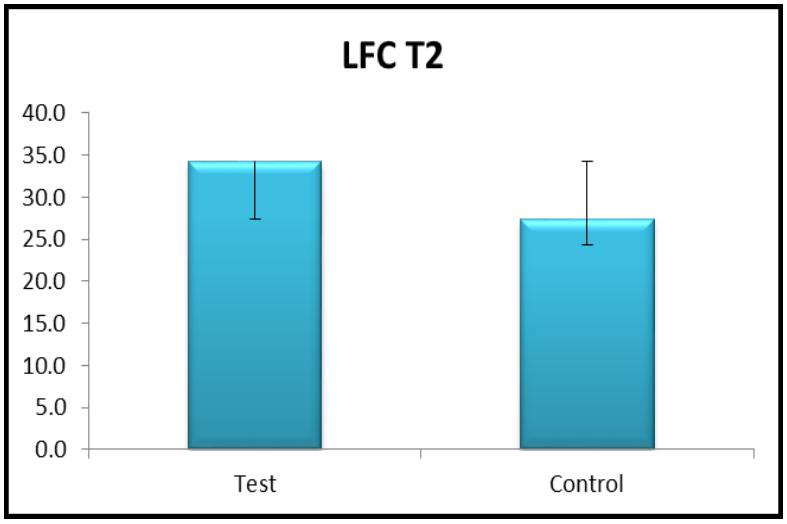
7.5 COMPARISON OF T2 VALUES AMONG THE TESTS AND CONTROLS OF THE STUDY GROUP :

T2 values are measured in five compartments, namely medial and lateral femoral condyle (MFC and LFC), medial and lateral tibial plateau (MT and LT) and patella (P). The following bar diagrams shows the comparison of T2 values in each compartment between the tests and controls.



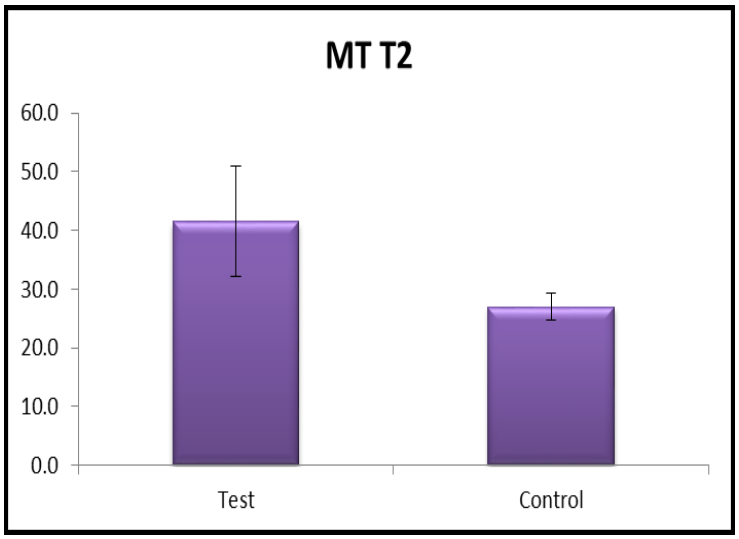
	AVERAGE T2
TEST	39.3±11.1
CONTROL	28.1±2.4

Fig 7.5.1 Bar diagram showing comparison of T2 values in medial femoral condyle among tests and controls of the study group.



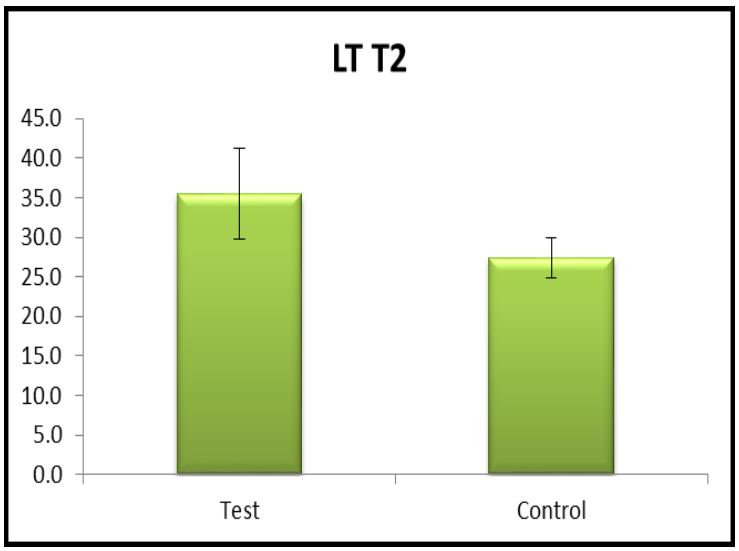
	AVERAGE T2
TEST	34.2±6.9
CONTROL	27.4±3

Fig 7.5.2 Bar diagram showing comparison of T2 values in lateral femoral condyle among tests and controls of the study group.



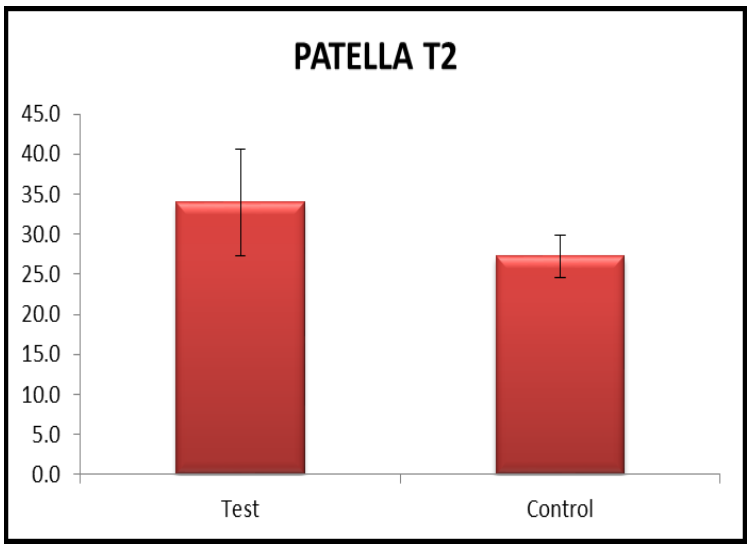
	AVERAGE T2
TEST	41.5±9.4
CONTROL	27.0±2.3

Fig 7.5.3 Bar diagram showing comparison of T2 values in medial tibial plateau among tests and controls of the study group.



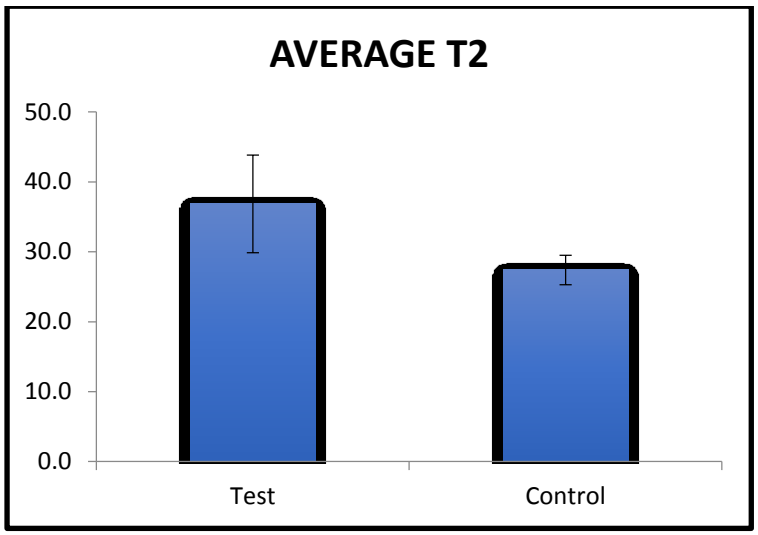
	AVERAGE T2
TEST	35.5±5.7
CONTROL	27.4±2.5

Fig 7.5.4 Bar diagram showing comparison of T2 values in lateral tibial plateau among tests and controls of the study group.



	AVERAGE T2
TEST	34±6.7
CONTROL	27.2±2.6

Fig 7.5.5 Bar diagram showing comparison of T2 values in patella among tests and controls of the study group.

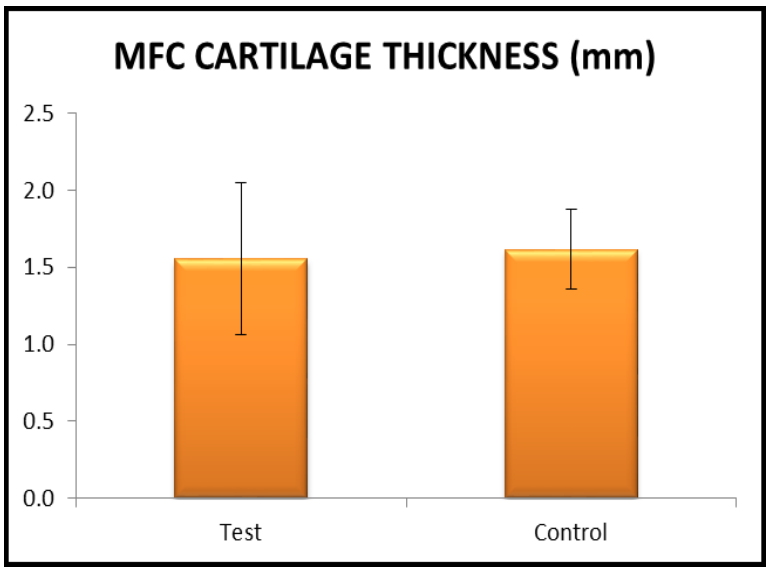


	AVERAGE T2
TEST	36.9±7.0
CONTROL	27.4±2.1

Fig 7.5.6 Bar diagram showing comparison of average of the T2 values in the five compartments among tests and controls of the study group.

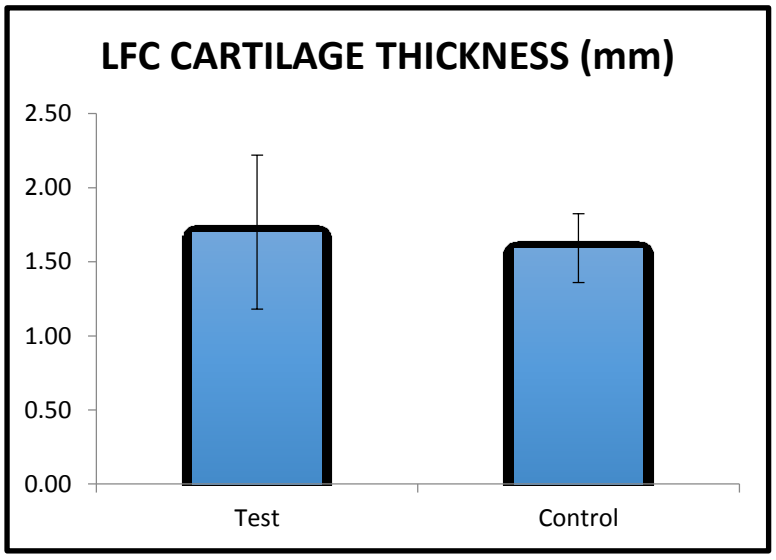
7.6 COMPARISON OF CARTILAGE THICKNESS AMONG THE TESTS AND CONTROLS OF THE STUDY GROUP :

Cartilage thickness is measured in five compartments, namely medial and lateral femoral condyle (MFC and LFC), medial and lateral tibial plateau (MT and LT) and patella (P). The following bar diagrams shows the comparison of cartilage thickness in each compartment between the tests and controls.



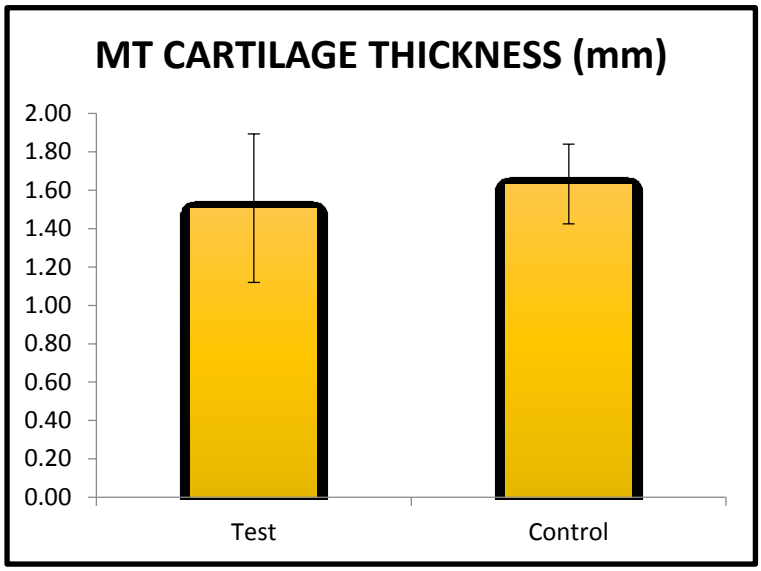
	AVERAGE CARTILAGE THICKNESS (mm)
TEST	1.6±0.5
CONTROL	1.6±0.3

Fig 7.6.1 Bar diagram showing comparison of cartilage thickness in medial femoral condyle among tests and controls of the study group.



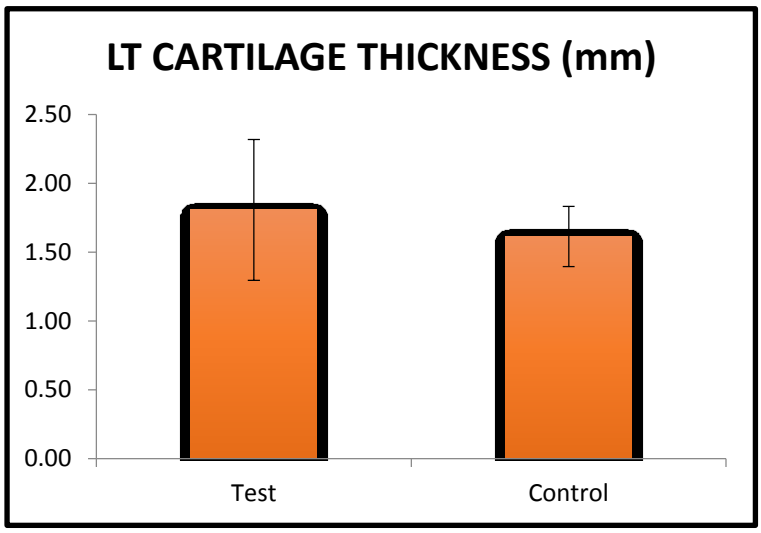
	AVERAGE CARTILAGE THICKNESS (mm)
TEST	1.7±052
CONTROL	1.59±0.23

Fig 7.6.2 Bar diagram showing comparison of cartilage thickness in lateral femoral condyle among tests and controls of the study group.



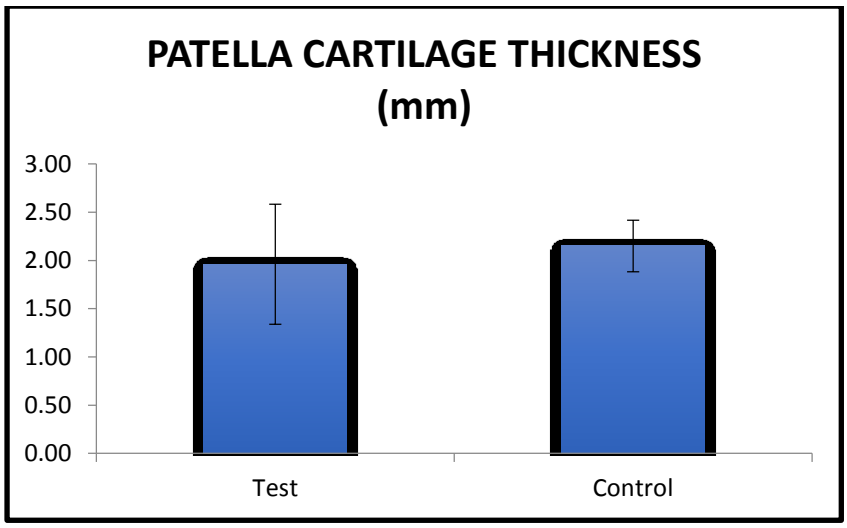
	AVERAGE CARTILAGE THICKNESS (mm)
TEST	1.5±0.39
CONTROL	1.63±0.21

Fig 7.6.3 Bar diagram showing comparison of cartilage thickness in medial tibial plateau among tests and controls of the study group.



	AVERAGE CARTILAGE THICKNESS (mm)
TEST	1.8± 0.51
CONTROL	1.61±0.22

Fig 7.6.4 Bar diagram showing comparison of cartilage thickness in lateral tibial plateau among tests and controls of the study group.



	AVERAGE CARTILAGE THICKNESS (mm)
TEST	1.96±0.62
CONTROL	2.1±0.27

Fig 7.6.5 Bar diagram showing comparison of cartilage thickness in patella among tests and controls of the study group.

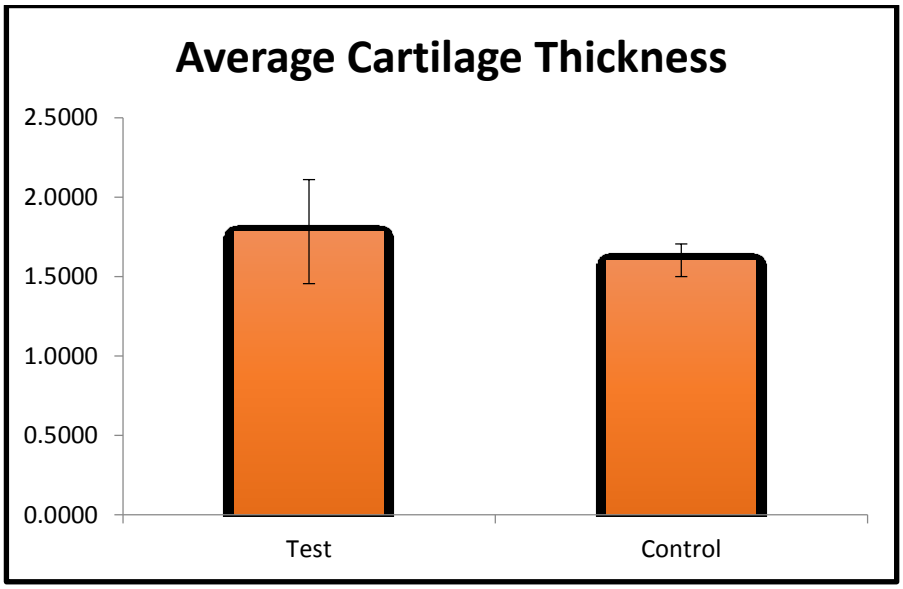


Fig 7.6.6 Bar diagram showing comparison of average of the cartilage thickness in the five compartments among tests and controls of the study group.

7.7 T TEST :

Group Statistics

Groups		N	Mean	Std. Deviation	Std. Error Mean
MFC T2	Test	15	39.273	11.0949	2.8647
	Control	25	28.140	2.3948	.4790
LFC T2	Test	15	34.207	6.8909	1.7792
	Control	25	27.380	3.0022	.6004
MT T2	Test	15	41.513	9.3741	2.4204
	Control	25	26.996	2.2649	.4530
LT T2	Test	15	35.45	5.703	1.473
	Control	25	27.41	2.524	.505
PATELLA T2	Test	15	33.993	6.6766	1.7239
	Control	25	27.248	2.6486	.5297
AVERAGE	Test	15	36.856	6.9647	1.7983
	Control	25	27.397	2.1033	.4207
MFC CT	Test	15	1.553	.4926	.1272
	Control	25	1.616	.2577	.0515
LFC CT	Test	15	1.700	.5196	.1342
	Control	25	1.592	.2326	.0465
MT CT	Test	15	1.507	.3863	.0997
	Control	25	1.632	.2076	.0415
LT CT	Test	15	1.807	.5120	.1322
	Control	25	1.614	.2187	.0437
PATELLA CT	Test	15	1.960	.6221	.1606
	Control	25	2.115	.2677	.0535
Average CT	Test	15	1.7827	.32784	.08465
	Control	25	1.6028	.10326	.02065

Above table shows the descriptive statistics of tests and controls.

7.8 INDEPENDENT SAMPLES TEST :

Independent Samples Test

		Equality of Variances		t-test for Equality of Means						
									the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
MFC T2	Equal variances assumed	68.380	.000	4.871	38	.000	11.1333	2.2856	6.5064	15.7603
	Equal variances not assumed			3.833	14.787	.002	11.1333	2.9045	4.9348	17.3318
LFC T2	Equal variances assumed	13.655	.001	4.341	38	.000	6.8267	1.5727	3.6430	10.0104
	Equal variances not assumed			3.635	17.240	.002	6.8267	1.8778	2.8690	10.7843
MT T2	Equal variances assumed	30.421	.000	7.448	38	.000	14.5173	1.9491	10.5717	18.4630
	Equal variances not assumed			5.896	14.987	.0005	14.5173	2.4624	9.2684	19.7662
LT T2	Equal variances assumed	13.258	.001	6.157	38	.000	8.045	1.307	5.400	10.691
	Equal variances not assumed			5.168	17.344	.0005	8.045	1.557	4.766	11.325
PATELLA T2	Equal variances assumed	17.457	.000	4.523	38	.000	6.7453	1.4914	3.7261	9.7646
	Equal variances not assumed			3.740	16.682	.002	6.7453	1.8034	2.9349	10.5558
AVERAGE	Equal variances assumed	36.384	.000	6.371	38	.000	9.4592	1.4847	6.4536	12.4648
	Equal variances not assumed			5.122	15.547	.0005	9.4592	1.8468	5.5348	13.3836

Above table shows the descriptive statistics regarding the T2 values in tests and controls which shows that there is a statistical significance. (P value < .05)

Independent Samples Test

		Equality of Variances		t-test for Equality of Means						
									of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
MFC CT	Equal variances assumed	4.380	.043	-.529	38	.600	-.0627	.1184	-.3023	.1769
	Equal variances not assumed			-.457	18.681	.653	-.0627	.1372	-.3502	.2249
LFC CT	Equal variances assumed	17.474	.000	.905	38	.371	.1080	.1194	-.1337	.3497
	Equal variances not assumed			.761	17.422	.457	.1080	.1420	-.1910	.4070
MT CT	Equal variances assumed	5.860	.020	-1.338	38	.189	-.1253	.0936	-.3149	.0642
	Equal variances not assumed			-1.160	18.940	.260	-.1253	.1080	-.3515	.1009
LT CT	Equal variances assumed	9.952	.003	1.657	38	.106	.1927	.1163	-.0427	.4281
	Equal variances not assumed			1.384	17.113	.184	.1927	.1392	-.1009	.4863
PATELLA CT	Equal variances assumed	16.211	.000	5.558	38	.000	.7867	.1415	.5001	1.0732
	Equal variances not assumed			4.647	17.161	.1890	.7867	.1693	.4297	1.1436
Average CT	Equal variances assumed	22.132	.000	2.559	38	.015	.17987	.07030	.03755	.32218
	Equal variances not assumed			2.064	15.684	.056	.17987	.08713	-.00514	.36488

Above table shows the descriptive statistics regarding the cartilage thickness in tests and controls which shows that there is a lack of statistical significance. (P value > .05)

RESULTS OF THE STUDY

1. The average T2 values were significantly higher in test subjects with OA when compared to controls without OA (36.9 ± 7.0 ms vs 27.4 ± 2.1 ms, P=0.0005) as shown in the above tables and bar diagrams.
2. Based on radiographs, three patients had a KL score = 1, four had a KL score = 2, five had a KL score = 3 and three had a KL score = 4.
3. Among the 15 OA patients, ten patients had more severe cartilage loss in medial compartments, two patients had more severe cartilage loss in lateral compartments and three patients had similar cartilage loss in both the compartments.
4. There were no significant differences in the average cartilage thickness in OA patients and controls.
5. There were no significant differences in the cartilage thickness for any compartment between OA patients and controls.
6. The average T2 values increased as KL scores increased based on x rays, with T2 values of 29.65, 32.58, 39.30 and 45.69 for KL scores 1,2,3 and 4 respectively.

8. DISCUSSION

Osteoarthritis is a non inflammatory degenerative joint condition. It is characterised by articular cartilage degeneration and new bone (osteophytes) formation. It is classified into two types, Primary and secondary.

Primary type is more common. It occurs in elderly, without any previous local joint pathology. It is mainly due to wear and tear changes in cartilage because of ageing. Secondary OA is due to a pre disposing cause like injury, infection, rheumatoid arthritis, hyperthyroidism, etc. Sitting cross legged and squatting are some of the reasons of increased prevalence of OA in India. In addition to changes in articular cartilage, OA also causes changes in ligaments and muscles. Due to low grade chronic inflammation, ligaments can undergo fibrous degeneration and muscles can undergo atrophy.

Advanced MR imaging sequences to evaluate the morphology of articular cartilage have evolved recently. 0.3 mm spatial resolution is needed to detect the superficial changes in cartilage, which is beyond the resolution of the morphological imaging sequences.

T2 mapping does not rely on spatial resolution to detect the cartilage damage. They depict the areas of increased water content and altered collagen matrix in the degenerated cartilage. Thus T2 mapping helps in detection of changes in cartilage composition and three dimensional ultrastructure of cartilage, before the morphological changes occur, thereby helping in early initiation of treatment.

In our study, we have demonstrated that the average T2 values in articular cartilage were significantly increased (P value =0.0005) in OA compared with controls without OA. Previously **Richard Kijowski MD et al.** [75] prospectively studied 150 subjects and found that increased T2 values in cartilages corresponded to cartilage lesions arthroscopically, especially in areas with more than two fold colour scale increase and areas which involved entire thickness of deep layer of cartilage. Thus the results of **Richard Kijowski MD et al.** [75] confirmed that increased T2 value in articular cartilage can be used as an indicator of cartilage degeneration in OA.

Previously **Mosher T et al. and Dunn TC et al.**[5,8,92] reported increased T2 values in cartilage in animal models and human subjects in vitro. The results of our study are consistent with the reported values – average T2 value of 36.9 for tests and 27.4 for controls. Poor correlation was noted between T2 values and proteoglycan (PG) concentration in previous in vitro studies [91]. Instead **Duvvuri et al. and Gray M et al.**[93,94] reported that collagen and water content and collagen orientation mainly affect T2 values.

Dunn TC et al.[8] correlated T2 values and disease severity of OA defined by KL scores, showing that T2 values were significantly elevated in mild OA (KL score = 1,2 n=20) compared with controls without OA. Similarly, in our study, T2 values increased with KL scores significantly (P value = 0.0005).

In our study, no significant difference was found in cartilage thickness between OA patients and controls. This lack of difference in cartilage thickness between OA patients and controls can be explained by the fact that the cartilage can get swollen due to an increase in water content in the early stages of OA and subjects with varying disease severity were included in the study group.

Our study has some advantages over some of the other compositional imaging techniques like dGEMRIC, sodium MR imaging, T1 mapping which require a long waiting time (several hour wait after contrast injection in dGEMRIC technique), use of intravenous contrast (in T1 mapping and dGEMRIC technique). In addition, our study does not require the use of special coil or contrast. Our study was done on a 3 Tesla MRI scanner as it offers increased SNR and increased resolution than other low field strength scanners.

9. LIMITATIONS OF THE STUDY

The limitations of our study are listed below :

1. Patients in our study could not be followed up for surgical or arthroscopic correlation of cartilage lesions. Arthroscopy is the reference standard for evaluating articular cartilage. So the exact diagnostic performance of T2 mapping could not be assessed.
2. Our study quantified the T2 values within the entire cartilage surface of the knee or in a specific compartment. It will be further useful to investigate the spatial variation of T2 within different layers of the cartilage, which may aid in better localisation of areas of cartilage degeneration.
3. T2 relaxation values are susceptible to the magic angle effect. T2 values will be inaccurate in those areas of the cartilage where collagen fibres are oriented at certain orientations to the external magnetic field.
4. Loss of proteoglycans occur prior to degradation of the collagen matrix in OA, therefore T2 mapping may not detect changes as early as techniques sensitive to GAG and PG content, like dGEMRIC or T1rho mapping.
5. Degree of joint loading was not standardised in patients participating in our study. The varying degree of joint loading in patients prior to examination may influence the T2 values in articular cartilage.
6. T2 relaxation time may be decreased in some areas of degenerated cartilage, because of additional sites of interaction with water molecules created by collagenase induced collagen cleavage.

10. CONCLUSION

Our study has shown that T2 mapping is a non invasive imaging technique that may improve our ability to detect early cartilage matrix degeneration, at the initial stage of pathogenesis of osteoarthritis i.e. collagen network alteration. Diagnosing cartilage damage prior to the detection by routine sequences that detect morphological cartilage lesions at a stage where the cartilage has already irreversibly damaged is potentially important in initiating early treatment and in monitoring disease progression in OA.

The addition of T2 mapping sequence to a routine MR imaging protocol can improve the sensitivity for detecting cartilage lesions. This is also useful for evaluation of cartilage in patients with unexplained knee pain without any meniscal tear and to evaluate the status of cartilage post cartilage repair and post arthroscopic surgery for internal derangement of knee.

To conclude, T2 mapping sequence can be used as a valuable tool to evaluate the articular cartilage, to detect cartilage lesions at an earlier stage in osteoarthritis which will be useful in planning the treatment strategies, thereby reducing and preventing the morbidity of osteoarthritis in the elderly.

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ABBREVIATIONS

MRI	-	Magnetic Resonance Imaging
OA	-	Osteoarthritis
DJD	-	Degenerative Joint disease
dGEMRIC	-	Delayed gadolinium-enhanced MR imaging of cartilage
GAG	-	Glycosaminoglycans
FSE	-	Fast spin echo
SE	-	Spin echo
SPGR	-	Spoiled Gradient Echo
PG	-	Proteoglycans
MCL	-	Medial Collateral Ligament
LCL	-	Lateral Collateral Ligament
ACL	-	Anterior Cruciate Ligament
PCL	-	Posterior Cruciate Ligament
AP	-	Anteroposterior
PA	-	Posteroanterior
FS PD FSE	-	Fat Supressed Proton Density Fast Spin Echo
GRE	-	Gradient Echo

SNR	-	Signal-to-Noise Ratio
NEX	-	Number of Excitations
FOV	-	Field Of View
KL	-	Kellgren and Lawrence
JSN	-	Joint Space Narrowing
DESS	-	3 D Dual Echo Steady State
bSSFP	-	3D Balanced Steady State Free Precession
DEFT	-	3D Driven Equilibrium Fourier Transform
SPACE	-	3D fast SE Sampling Perfection with Application-optimized Contrast using different flip-angle Evolutions
IDEAL	-	Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation
STIR	-	Short Tau Inversion Recovery
PD	-	Proton Density
FLASH	-	Fast Low-Angle Shot
True FISP	-	Fast Imaging with Steady-state Precession
FIESTA	-	Fast Imaging Employing Steady-state Acquisition
Balanced FFE	-	Fast Field Echo
FEMR	-	Fluctuating Equilibrium MR
Gd-DTPA	-	Gadolinium DiethyleneTriaminePentaacetic Acid
RF	-	Radio Frequency
TR	-	Time of Repetition

TE	-	Time of Echo
FOV	-	Field Of View
NEX	-	Number of Excitations
MFC	-	Medial Femoral Condyle
LFC	-	Lateral Femoral Condyle
MT	-	Medial Tibia
LT	-	Lateral Tibia
ROI	-	Region Of Interest

PATIENT PROFORMA

STUDY TITLE:

"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''

Sl. No:

Name:

Age/Sex:

Occupation:

Address:

Presenting Complaints and History:

Data Collection Proforma :

REGION	AVERAGE T2 VALUE	AVERAGE CARTILAGE THICKNESS	KL SCORE
MFC			
LFC			
MT			
LT			
PATELLA			

PATIENT INFORMATION SHEET

"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''

- Your cooperation would be valuable to us for the same
- The privacy of patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part of the study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.
- The result of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of the investigator Signature of participant

Date:

PATIENT CONSENT FORM

STUDY TITLE:

"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''

PARTICIPANT NAME : Age: Sex: OP/ IP.NO. :

I confirm that I have understood the purpose of procedure for the above study.I have the opportunity to ask the questions and all my questions and doubts have been answered to my satisfaction.I have been explained about the pitfall in the procedure.I have been explained about the safety,advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I'm free to withdraw at any time without giving any reason. I understand that investigator,regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it,even if I withdraw from the study.I understand that my identity will not be revealed in any information released to third parties or published,unless as required under the law.

I HEREBY CONSENT TO UNDERGO COMPLETE PHYSICAL EXAMINATION, BIOCHEMICAL AND RADIOLOGICAL INVESTIGATION PERTAINING TO THE STUDY.

Signature/Thumb Impression of Participant

ஆராய்ச்சி தகவல் தாள்

காந்த அதிர்வு அலை வரைவின் (எம்.ஆர்.ஐ) பல்வேறு வரிசைகளைப் பயன்படுத்தி முழங்கால் மூட்டு எலும்பு தேய்மானம் (கீல்வாதம்) குறித்த முழங்கால் மூட்டு எலும்பு ஜவ்வு ஆய்வு

இந்த ஆய்வு மூலம் கண்டறியப்படும் முழங்கால் மூட்டு எலும்பு ஜவ்வு மாற்றங்களை வைத்து முழங்கால் மூட்டு எலும்பு தேய்மானத்தை முன்கூட்டியே கண்டறியலாம் என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வில் முழங்காலுக்கு எடுக்கப்படும் எம்.ஆர்,ஐ ஸ்கேன் மூலம் எந்த பக்க விளைவுகளும் ஏற்படாது.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்

இந்த சிறப்பு ஆய்வின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராயிச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்: பங்கேற்பாளர் கையொப்பம்:

நாள்:

இடம்:

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு

காந்த அதிர்வு அலை வரைவின் (எம்.ஆர்.ஐ) பல்வேறு வரிசைகளைப் பயன்படுத்தி முழங்கால் மூட்டு எலும்பு தேய்மானம் (கீல்வாதம்) குறித்த முழங்கால் மூட்டு எலும்பு ஜவ்வு ஆய்வு

பெயர்	:	தேதி	:
வயது	:	உள்நோயாளி எண்	:
பால்	:	ஆராய்ச்சிசேர்க்கை எண்	:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த அராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பதின் பேரில் பங்கு பெறுகின்றேன்.

இந்த ஆரய்ச்சியில் இருந்து நான் எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் எற்படாது என்பதையும் நான் புரிந்து கொண்டேன்.

நான் இந்த ஆராய்ச்சியின் விபரங்களைக் கொண்ட ஆராய்ச்சித் தகவல் தாளைப் பெற்றுக்கொண்டேன்.

இதன் மூலம் எந்த பின் விளைவும் எற்படாது என்று மருத்துவர் மூலம் தெரிந்து கொண்டு, நான் என்னுடைய சுயநினைவுடனும் மற்றும் முழுசுதந்திரத்துடனும் இந்த மருத்துவ அராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதம் தெரிவிக்கிறேன்.

தேதி :

பங்கேற்பாளர் கையொப்பம்

MASTER CHART

CASES															
				T2						CARTILAGE THICKNESS (mm)					
S NO	AGE	SEX	KL SCORE	MFC	LFC	MT	LT	PATELLA	AVERAGE	MFC	LFC	MT	LT	PATELLA	Average
1	52	M	3	44.2	31.5	41.5	29	25.5	34.4	1.6	2.3	2.3	2.9	2.1	2.24
2	50	M	4	56	32.5	50.2	32.2	31.5	40.5	1.7	1.3	1.3	1.6	3.6	1.9
3	68	F	4	52.2	42	51.3	45.8	39.5	46.16	0.8	1.9	1.2	2.1	2.4	1.68
4	65	M	4	57.4	48.5	54.6	46.2	45.6	50.42	1.6	2.5	1	1.6	2	1.74
5	46	M	1	30.5	30	29.3	28	32.5	30.06	2.7	1.8	1.3	2.6	3.2	2.32
6	48	M	1	28.5	26.2	36.5	30.7	31.6	30.7	2.1	1.4	2	2.3	2.7	2.1
7	54	F	3	40.2	38.5	42.6	39.2	37	39.5	1.3	2.5	1.6	2	1.8	1.84
8	47	F	2	26.5	32.5	38.5	35.2	36.1	33.7	0.8	1.9	1.5	1.4	1.9	1.5
9	48	F	2	28.5	39.5	26.2	38.6	36.1	33.7	1.8	2.3	1.3	1.9	3	2.06
10	49	F	2	35.2	32.2	38.6	34.2	27.2	33.4	1.7	1.4	2.2	1.7	3	2
11	65	F	2	30.8	27.2	35.1	29.2	25.9	29.5	1.8	1.4	1.4	1.6	2.4	1.72
12	49	F	3	31.2	31.8	39.2	34	30.7	33.3	1.3	1.2	1.2	1.1	1.9	1.34
13	45	F	3	48.8	38.6	51.4	40	38.3	43.4	1.7	1.3	1.7	1.8	2	1.7
14	60	F	3	49.7	40	56.2	37.4	46.3	45.9	1.4	0.8	1.4	1.4	1.5	1.3
15	50	F	1	29.4	22.1	31.5	32.1	26.1	28.2	1	1.5	1.2	1.1	1.7	1.3
CONTROLS															
16	26	F	0	25.4	21.6	24.6	20.3	20.5	22.4	1.6	1.3	1.4	2.1	1.8	1.64
17	34	F	0	28.1	30	27.9	26	27.4	27.8	1.8	1.4	1.5	1.9	1.3	1.58
18	16	F	0	24.5	19.2	20.1	22	21.1	21.3	2	1.4	1.5	1.5	1.1	1.5
19	18	M	0	30	27.2	28.1	26.3	29	28.1	1.7	1.3	1.9	1.4	1.9	1.64
20	44	M	0	26	26.5	28.4	26	29.1	27.2	1.9	1.7	1.7	1.6	1.5	1.68
21	35	F	0	31.1	28	28.7	29	29.5	29.2	1.2	1.5	2.1	1.8	1.4	1.6
22	37	F	0	30.2	30	26.7	27	25.1	27.8	1.3	1.9	1.6	1.8	1.6	1.64
23	26	M	0	26	27.5	27.6	26.1	25	26.4	1.5	1.5	1.5	1.5	1.5	1.5
24	26	M	0	24	22.5	23.1	26	26.3	24.3	1.9	1.4	1.8	1.6	1.7	1.68
25	18	M	0	33	29.2	26	28.2	29.4	29.1	1.6	1.2	1.5	1.4	1.6	1.46
26	23	M	0	29.1	28.7	25	28.6	27.4	27.7	1.7	2	1.3	1.65	1.5	1.63
27	32	M	0	25.5	28	29.3	25.6	27	27.08	1.2	1.9	1.6	1.6	1.2	1.5
28	16	F	0	29	30.4	28.6	28.2	29.3	29.1	1.4	1.6	1.7	1.4	1.8	1.58
29	29	F	0	28.5	26.3	28.6	29.5	31.3	28.8	1.9	1.4	1.9	1.8	1.9	1.78
30	40	M	0	29.5	28.2	29	32	27.1	29.1	1.9	1.8	1.9	1.8	2	1.88
31	26	M	0	27.1	29.3	28.2	28.6	26	27.8	1.6	1.7	1.4	1.7	1.8	1.64
32	35	F	0	28.3	30.5	26	29.5	29	28.6	2	1.5	1.5	1.5	1.6	1.62
33	32	M	0	26	25.2	24.3	28.4	28.1	26.4	1.7	1.9	1.8	1.3	1.2	1.58
34	31	M	0	31	29.5	29	28.4	28.2	29.2	1.4	1.7	1.6	1.6	1.4	1.54
35	25	M	0	29.2	28	28.5	27.6	26.6	27.9	1.8	1.4	1.4	1.2	1.3	1.42
36	29	M	0	27.4	26	26.2	29	29.3	27.5	1.5	1.6	1.8	1.9	1.3	1.62
37	36	F	0	32	30.6	26.5	27.1	28.3	28.9	1.1	1.3	1.5	1.9	1.4	1.44
38	24	F	0	29	26.1	28.2	31.8	30	29.02	1.6	1.8	1.6	1.5	1.7	1.64
39	25	M	0	25.2	24.6	26.3	26.8	23.1	25.2	1.4	1.7	1.9	1.4	2.1	1.7
40	29	M	0	28.4	31.4	30	27.2	28.1	29.02	1.7	1.9	1.4	1.5	1.4	1.58

ETHICS COMMITTEE APPROVAL LETTER

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.G.Harish
I Year PG in MD RD
Barnard Institute of Radiology
Madras Medical College
Chennai 600 003

Dear Dr.G.Harish,

The Institutional Ethics Committee has considered your request and approved your study titled **"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI " - NO.30052017**

The following members of Ethics Committee were present in the meeting hold on **02.05.2017** conducted at Madras Medical College, Chennai 3

1.Prof.Dr.C.Rajendran, MD.,	:Chairperson
2.Prof.R.Narayana Babu, MD.,DCH.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
4.Prof.S.Suresh,MS.,Prof.of Surgery,MMC, Ch-3	: Member
5.Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
6.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
7.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
8.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-6

PLAGIARISM ANALYSIS REPORT

URKUND

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T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI"

1.

INTRODUCTION

Osteoarthritis (

OA) is the most prevalent chronic disease in the elderly. Osteoarthritis is a disease attributed to multiple etiological factors and is characterized by progressive degeneration and eventual loss of cartilage tissue(1). OA is still poorly understood, which may be attributed to the fact that it is generally detected at an advanced stage.

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"T2 MAPPING OF ARTICULAR CARTILAGE IN OSTEOARTHRITIS OF THE KNEE USING 3 T MRI''** of the candidate **Dr.HARISH.G** with registration Number **201618002** for the award of **M.D RADIODIAGNOSIS** in the branch of **VIII**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **5 percentage** of plagiarism in the dissertation.

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